BUREAU OF HYGIENE AND TROPICAL DISEASES

BULLETIN OF HYGIENE

Volume 34, No. 11 November 1959

Public Health

BROCKINGTON, C. F. **Public Health at the Privy Council, 1858–71.** *Med. Officer.* 1959, Mar. 26, Apr. 3, 10, 17, May 1, 8, 15 & 22, v. 101, Nos. 13, 14, 15, 16, 18, 19, 20 & 21, 173–7; 185–90; 197–200; 211–15; 243–6; 259–60; 278–80; 287–90, 13 figs. [Refs. in footnotes.]

This valuable excursion into English public health history is serialized in 8 issues. It describes that hitherto neglected period of the history of public health in England when central authority was vested in the Privy Council. It opens 4 years after the dismissal with contumely of Edwin Chadwick and closes with the establishment of the Local Government Board whose work came to an end in 1919 when the Ministry of Health began.

The Privy Council provided a quiet backwater in which scientific problems could be properly studied. The man responsible for their study was Sir John Simon who, after holding office as the first MOH of the City of London, had acted as adviser of the defunct Board of Health and remained in the government service after Chadwick's departure. He gathered together a brilliant team whose achievements are set out in these articles, the compilation of which must have involved much arduous research by the industrious author. The work of this team, whose names are unknown to most people today, laid the foundations on which public health law and practice are built.

Part II which appears in the issue of April 3 describes in some detail the various surveys. They cover a wide field and include "The Alvine Flux", diphtheria and industrial diseases. Guy investigated arsenical colouring in artificial flowers and wallpaper: Bristowe the use of red phosphorus in matches: Edward Smith conducted dietetic, and Julian Hunter housing, surveys.

Part III (April 10) deals with the "Tendance of Infants" and reveals rates of infant mortality of 333 for illegitimate and 250 for legitimate children and the almost universal use of opium as a children's quietener. This part also comments on enquiries into epidemics and vaccination. There is an account of Thudichum's investigation into parasitic disease in meat and of Wagstaffe's into venereal disease.

As a result of these surveys the Sanitary Act of 1866 was passed and after that Simon agitated for an effective means of enforcing it centrally and locally. This led to the establishment of the Local Government Board and of the local sanitary authorities, between them covering the whole country, though their performance did not reach Simon's expectation.

The team numbered 17, some part-time, others whole-time at £800 a year. With 3 exceptions, Guy, Greenhow and Seaton, they were all, at the time of their appointment, young and inexperienced. They were, in fact, appointed on the basis of a brilliant student career plus an interest in sanitary science. Their performance came up to their promise: 8 became fellows of the Royal Society and 5 censors of the Royal College of Physicians. Their background was varied and they illustrate Simon's superb capacity for personnel selection. The early days of the Epidemiological Society, now a section of the Royal Society of Medicine, are briefly described.

Interesting biographical details and photographs of these pioneers are given. Dr. W. A. Guy was in turn Professor of Forensic Medicine and of Hygiene at King's College, London and became President of the Statistical Society. Dr. E. H. Greenhow had been in general practice in Tyneside where he became Chairman of the Tynemouth Board of Health during an epidemic of cholera. On moving to London he continued clinical practice and was appointed part-time unpaid Lecturer in Public Health at St. Thomas' Hospital. He later was a full physician at the Middlesex Hospital. He travelled widely on official duty and was a pioneer in medical statistics. Dr. E. C. Seaton was an authority on vaccination and became Chief Medical Officer of the Local Government Board in 1876 when Simon retired. Dr. George Whitley was a linguist and is chiefly remembered for his translations into English of French and German medical classics. He was sent by Simon to Russia to investigate epidemic diseases in that country and there is evidence that he knew Russian also.

The memory of Sir John Simon will always remain green. It is, perhaps, not generally known that throughout his public health career he was an active member of the staff of St. Thomas' Hospital first as pathologist and later as surgeon. While MOH of the City of London he had a private surgical practice and

gave it up only when he joined the service of the government. Like many of the public health pioneers he was long-lived and was 88 when he died. In 1887, 11 years after his retirement at the age of 60, he was created K.C.B.

Part V (biographical detail) is continued in succeeding numbers. That of May 1 deals with Edward Smith, E. A. Parkes, H. J. Hunter and Henry Stevens: that of May 8, J. S. Bristowe, J. Burdon Sanderson and J. L. W. Thudichum: in that of May 15 we find information about J. N. Radcliffe and George Buchanan and on May 22 about W. M. Ord, Richard Thorne and W. W. Wagstaffe.

The series concludes with a list of the published surveys and reports of each member of the team.

The outstanding impression given by reading these "lives" is that, unlike most public health workers of today, the men were actively engaged in clinical work while pursuing their public health enquiries. Their energy was prodigious.

This series is a connected whole and is too useful to be spread over 8 issues of a journal. The journal is to be congratulated on realizing their value and finding space for them but it is to be hoped that the articles will eventually appear as a book.

Allen Daley

BROWN, J. R. & THORNTON, J. L. **William Odling as Medical Officer of Health to Lambeth 1856–60.** *Med. Officer.* 1959, Aug. 21, v. 102, No. 8, 77–8.

This is another in the important series of biographical sketches of the founders of the British public health service now appearing in this journal. Most of these pioneers are unknown to-day even by name and it is fitting that their work should be put on record.

William Odling was born in Southwark in 1829 and died in 1921. He is another example of the longevity of the social reformers of that period. He was primarily a chemist and, after holding chemical posts at Guy's and St. Bartholomew's Hospitals, eventually in 1872 was appointed Waynflete Professor of Chemistry at Oxford; a position which he held for 40 years. He was a fellow of the Royal Society and of the Royal College of Physicians.

He was appointed MOH by the Lambeth Vestry in 1856 at a salary of £400 a year: this was reduced to £300 within a year and the office was discontinued altogether in 1860 when he was appointed Chemical Examiner of Gas in Lambeth. The suggestion is made that though he executed his duties with vigour he devoted an undue amount of time to his chemical interests.

During his tenure of office, cholera was present in his district and the pollution of, and stench from, the Thames was described as "a scandal". Odling reported against the proposed use of perchloride of iron as a deodorant. A court case against a size manufacturer in which he had appeared as an expert witness before his appointment as MOH is described.

He was one of the founders of the Metropolitan Association of Medical Officers: he advocated the provision of water for every house and the construction of drains and sewers: he examined samples of flour and bread and was active in the early campaigns against adulterated food.

Allen Daley

DENSEN, P. M., SHAPIRO, S. & EINHORN, Marilyn. **Concerning High and Low Utilizers of Service in a Medical Care Plan, and the Persistence of Utilization Levels over a Three Year Period.** *Milbank Memorial Fund Quarterly.* 1959, July, v. 37, No. 3, 217–50, 4 figs.

The first objective of this study was to determine the extent to which individuals who are heavy users of physician services in one year remain heavy users in succeeding years, and whether low users remain low users consistently. The second was to establish whether certain characteristics could be used to identify subgroups with an unusually high usage. The third was to determine whether family units show any greater or lesser consistency in their year-to-year pattern than do individuals.

The analysis was based on records kept by physicians relating to City of New York employees in the Health Insurance Plan of Greater New York (HIP)—a voluntary prepaid plan providing comprehensive medical care on a group practice basis.

In 1954, 13·7% of the patients had 10 or more services from physicians, and accounted for 52·4% of the physicians' services. However, only 2·9% were consistent high users over the 3 years 1954–6, accounting for 13·3% of the physicians' services. These high users were not found to be abnormally clustered in a small number of families. However, there were more adults aged 45–59 and aged 60 and over than among patients who used the physician less. The authors suggest that the next step must be a clarification of the medical conditions for which care is received by the high users, together with an assessment of the degree to which this care is supportive or directed at somatic conditions.

Margot Jefferys

HRUBEC, Z. **The Association of Health and Social Welfare Problems in Individuals and their Families.** *Milbank Memorial Fund Quarterly.* 1959, July, v. 37, No. 3, 251–76, 2 figs.

Data obtained in a community health survey and from community agencies have been used to test the hypothesis that there are more social problems, unrelated to health, in the families of individuals with health problems than there are among families where none of the individual members have serious health problems.

The health data were obtained in interviews conducted with responsible adults from a random sample of 2,370 families living in the Arsenal Health District in Pittsburg during 1951 and 1952. A health problem was defined as an illness during the past month, an accident or injury or hospitalization during the past year or a chronic disease or physical impairment of long standing. A social problem was said to exist if an individual was known to one of 105 social agencies. 4 types of social problem were distinguished: those which arose primarily from an existing health problem; those where a person's social behaviour produced a need for a social service; those where there

were both health and social reasons for contact with a social agency; and, finally, those which did not fit into any of these categories.

When age was taken into account, the men with both health and social reasons for contact with a social agency, and women with health reasons only, reported illness more frequently than other groups. Men with social reasons only reported illness less frequently than those with no contact with social agencies at all.

Neither the individuals with social reasons nor those with health reasons were randomly distributed among families. There were more families than expected with no such individuals and more with two or more such individuals. Moreover, in families where illness was reported the healthy members more frequently had social reasons for contact with an agency, than was the case in families reporting no illness.

In enquiries of this kind, definitions are of supreme importance, and the significance of the findings must always be judged in the light of the arbitrary definitions which have necessarily to be made. Nevertheless, medical men and social workers have commented frequently on the apparent clustering of health and social problems in particular families. This study has merit because it underlines the need to avoid facile conclusions based on tautological arguments.

Margot Jefferys

Maternal and Child Health

BURDEN, Jennifer K. **A Study of Demand Feeding and Rooming-In of Babies.** *Med. J. Australia.* 1959. Apr. 18, v. 1, No. 16, 520–27.

The author is a social worker and the study was made on 513 women confined at the Queen Elizabeth Hospital, Adelaide between August 1957 and March 1958. Different routines for feeding the babies and for nursery care or "rooming-in" with the mothers were adopted on the different floors of the hospital and this provided 4 groups which could be compared.

The objective test, as between demand and routine feeding, used was the proportion of the babies who regained their birth weight by the 7th day. On rooming-in the mothers were asked while in hospital and again 6 weeks after discharge and while attending the post-natal clinic, for their opinion about (a) rooming-in by day only, (b) rooming-in day and night, and (c) nursery control of the babies.

The results of the study are: of babies who were demand fed and roomed-in day and night 60% regained their birth weight by the 7th day; of babies on demand feeding in the daytime and nursery control at night, 35% regained their birth weight by the 7th day; the lower the birth weight (premature babies excluded) the greater was the tendency to regain the birth weight by the 7th day irrespective of the feeding schedule; more women practised demand feeding 6 weeks after delivery than during the first week; routine-fed babies dispensed with the night feed earlier than did the demand-fed babies. Of the 20 babies which were artificially fed, 6 regained their birth weight by the 7th day.

Many of the mothers knew nothing about the rooming-in practice of the hospital until after admission. This is felt to be wrong. They should all be told before admission.

The conclusions on this section of the enquiry are: of the women in the study 95% were in favour of rooming-in when interviewed in the hospital; views at the enquiry 6 weeks after discharge showed little change; approximately 60% of private and ward patients (4-bedded units) rooming-in day and night denied any disturbance at night; 82% of the women denied that caring for their own baby was in any way too tiring or difficult; of the 20 fully nursery-managed babies 14 developed some clinical infection compared with 119 of the 464 rooming-in with their mothers; the majority of infections developed between the 2nd and 6th days.

The educational value of rooming-in is considerable and the conclusions are: of primiparae interviewed at the post-natal clinic 6 weeks after the birth 89% stated that they had returned home with confidence and were well educated to care for their baby; of multiparae questioned at the post-natal clinic 72% stated that they had greater confidence with the roomed-in baby than with previous babies; there was less post-natal depression when mothers had their babies beside them; fathers preferred rooming-in of the babies. *Allen Daley*

LEWIS, J. B. **A Study of the Health of a Pre-School Age-Group in an African Urban Community.** *J. Trop. Pediatrics.* London. 1959, June, v. 5, No. 1, 10–21, 2 figs.

The community studied was predominantly Zulu, living in a municipal housing estate on the outskirts of Durban. Hygienic conditions were good, comprising permanent houses, a piped water supply, water-borne sewage and adequate surface drainage, while pasteurized milk, fresh meat and fresh vegetables were available. Into this satisfactory environment, however, a constant influx of relatives and friends from primitive rural areas carried infection, insanitary habits and a population far in excess of that desirable. The study was made by the staff of the Institute of Family and Community Health in Durban, and the paper opens with a review of studies already carried out in South Africa on the growth patterns of the child population [see, for example, this *Bulletin*, 1953, v. 28, 1009].

The heights of Bantu children are lower than those of both the upper and lower white income groups, though the growth curve of the lower white income

group boys is within ½ standard deviation of that of Bantu boys, while the growth curve of white girls of the same social group runs at ½ standard deviation above that of the Bantu girls.

While white children of both sexes belonging to upper income groups are significantly heavier than the other two groups, there is no difference in the rate of weight increment between the lower income group white and the Bantu children.

Morbidity studies were based on the attendance of the children at the Institute in 1954: out of a population in the 2–5 years age-group numbering 2,427, 1,193 attended and 1·6 diagnoses per child were made. Of the diseases recorded, those due to air-borne infection contributed 76·4%, excremental infection 33·8% and physical contact 23·2% of the whole. Nutritional diseases showed the low incidence of 17·5% [although voluntary attendance at a clinic is likely to cause selection of the better elements in the population, who do not represent the nutritional status of the childhood population in general].

Posture was classed as "poor" in 76%, fair in 22% and good in 2%; these figures reflect the influence of recurrent illness and undernutrition.

Emotional and behaviour disturbances did not seem to present any problem in Bantu children at this age.

The mortality rate for this age-group in the years 1953–7 was, as far as could be ascertained in an unstable population, 5·36 per 1,000. The cause of death was unknown in 36·2%; tuberculosis (12 deaths), pneumonia (9 deaths) and gastro-enteritis (6 deaths) appeared to provide the greatest risk to child life.

The average income of a male worker, of whom the majority were employed as unskilled labourers, was £2–£2 10 0 per week; this low wage compelled the mother to seek work also in most families, to the inevitable neglect of her children. Urbanization tends to break tradition and family ties, children are often sent away to be cared for by grandparents or other relatives and illegitimacy is frequent.

The diet of the community is mainly carbohydrate, the staple cereals being maize-meal and rice with potatoes, while supplements of green vegetables, milk, fish, meat and fruit are also eaten though usually in amounts which are inadequate.

Much illness is attributed to witchcraft, and this belief adds much difficulty to the already formidable task of the social worker and the public health authority.

[This article indicates some of the problems which arise in an African population subjected to rapid urbanization even under favourable conditions.]

J. H. Walters

COOK, N. J. **Starting School: a Socio-Medical Problem.** *Med. Officer.* 1959, June 19, v. 101, No. 25, 337–40, 3 figs.

This study is from the Hengrove Child Health Centre and a general practice in Bristol.

The records of 236 girls and 216 boys who had been registered with the practice during the whole of their sixth year of age within the period 1948 and 1955 were examined.

The illness experience in any one year varies and depends on the incidence of the infections with a biennial cycle. 11 tables analyse the data in various ways. The first child in a family has more illness on starting school than those with elder brothers or sisters: only children had on the average 4·87 illnesses during their sixth year compared with 4·26 among the first born in a family of 2 and 2·83 in a family of 4: the incidence varies with the school; the highest was in a small private school but here the real reason may be that medical aid was sought more readily.

The commonest reasons for the doctor being consulted were respiratory, infectious and parasitic diseases. "About 80 per cent. of the disease suffered by the child in his first year at school is due to infection of some sort or other."

An important table gives *rates* of illness per 1,000 children at risk for their 5th, 6th and 7th years. For all diseases combined and for each sex the 6th year was the highest. With the single exception of whooping-cough more cases occur in the 5-year-olds than in the other 2 age-groups. Even in whooping-cough the number of cases among the 5-year-olds is exceeded only by those aged 3. The commonest age for urticaria, gastroenteritis, accidents and lower respiratory infections is 2: for septic skin conditions, upper respiratory infections, tonsillitis and pharyngitis and otitis media it is 5.

The question is discussed whether this increase of illness on starting school matters. The inference is that it does and that many cases of chronic sinusitis and recurrent bronchitis originate in the heavy exposure met in schools. More hygienic school buildings and smaller classes ought to reduce the amount of illness due to starting school.

It is pointed out that this is not a study of *all* illnesses affecting the children but only of those where the family doctor was consulted. Both parental anxiety and the seriousness of the illness are factors in determining whether or not medical aid is sought.

Allen Daley

GODDARD, J. L. **Accident Prevention in Childhood.** *Pub. Health Rep.* Wash. 1959, June, v. 74, No. 6, 523–34, 2 figs.

In this paper on the prevention of accidents in children the author first defines the magnitude of the problem by quotation of the statistics from the Western Hemisphere where accidents are the leading cause of death in children 5 to 14 years of age in 13 of the constituent countries. Data on the 5 principal causes of death in the 17 countries of the Americas and Puerto Rico, Jamaica and Trinidad with rates per 100,000 population, for children in the 2 age-groups, 1–4 and 5–14 years, for 1956 are clearly set out in 2 figures. There is a great geographical variation in the relative significance of accidents as a cause of mortality and morbidity. Only in the United States and Canada were accidents the leading cause of death in the 1–4 age-group and in only 8 of the other countries were accidents even listed among the 5 leading causes of death since they are so greatly outnumbered by disease deaths. In the 5–14 age-group, however, accidents are

the leading cause of death in two-thirds of the reporting countries. There are tables which set out particulars of the actual number of deaths from accident in children with rates per 100,000 in the Americas and the number of these deaths by sex, age and type of accident. There is detailed consideration of accidental poisonings in children.

In a long discussion of the prevention of accidents particular stress is placed on (1) the need for more information to be obtained by a good accident reporting system and by specific researches, (2) education by public health agencies, physicians and school teachers, (3) proper coordination of activities and (4) improved legislation for example in the regulation of inflammable fabrics for children's clothes. There is also some account of "secondary prevention" by which is meant the amelioration of the effects of accidents by improvement of emergency services and the early application of methods of rehabilitation.

M. E. Delafield

HAGGERTY, R. J. **Home Accidents in Childhood.** *New England J. of Med.* 1959, June 25, v. 260, No. 26, 1322–31, 7 figs. [48 refs.]

This is a clear general and statistical account of the problem of home accidents in childhood in the United States where in 1956 the total of all deaths from accidents in children from 1 to 14 years of age was over 10,000. After the first year of life accidents come easily first in the list of causes of death. Home accidents account for 38% of all accidental deaths in children under 15 years of age and 58% in the under 5 age-group. It is estimated that 150 to 200 children are non-fatally injured for each accidental death and of these 1 in 40 is left permanently crippled. The statistics are analysed and described at some length. Figures set out the leading causes of death among children, accidents expressed as a percentage of all deaths, accidents by age and place of accident, types of accidents and number of injuries per 100 persons per year and fatal home accidents according to the nature of the injury by age. The emergency treatment of common home accidents and their prevention together with the role of the individual physician in accident prevention are discussed at some length. It is considered that a very considerable amount of research on home accidents is yet to be done and a list of the community-based and individual studies which are in progress is given.

"The concept that best expresses the present state of knowledge concerning accident aetiology is that of multiple causation, in which the variables of host, environment and agent all play a part in each accident, but the importance of each of these factors varies from accident to accident."

M. E. Delafield

Care of Old Persons and the Chronically Ill

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. NO. 171. **Mental Health Problems of Aging and the Aged. Sixth Report of the Expert Committee on Mental Health.** Geneva. 1–6 September 1958. 51 pp. 1959. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [3s. 6d.; $0.60; Sw.fr. 2.–.]

This report is the work of an expert committee of 6 and a secretariat of 4. The latter included Dr. E. E. KRAPF, the Chief Medical Officer of the Mental Health Division of WHO and Professor Martin ROTH of Newcastle-upon-Tyne.

The chapters deal with the extent of the problem, its sources, the protection and promotion of mental health in old age, the classification and prognosis of mental disease in old age, organisation of geriatric mental health services, specific treatment measures, rehabilitation, training of personnel and organization of research.

A general conclusion is that much more information is needed on why the aged become mentally ill. This involves research and 10 separate subjects for enquiry are set out. Institutes of gerontology would be useful in this connexion.

The sources of mental illness among the aged are discussed under the headings socio-economic, psychological, psychopathological and physical factors.

The demand for more hospital care arises from (1) deterioration in home care (2) more people survive to old age and (3) hospitals have a better reputation. It is often a combination of physical and mental illness which leads to a demand for admission. Swedish experience shows that there has been no change in the incidence of senile psychosis in that country in the last 25 years.

A relatively high proportion, 40 to 50%, of mental illnesses in old people are now regarded as curable.

It is strongly recommended that for each district there should be a single public health organization for planning, directing and developing a combined preventive and therapeutic service.

A Geriatric Guidance Centre should be established as the focal point of any scheme and there should be associated with it a short-term in-patient unit, a day hospital, a long-stay hospital, residential homes and a mental hospital.

Professor A. QUERIDO of Amsterdam was a member of the Expert Committee and much that is advocated is already in operation in that city.

For each patient there should be a domiciliary conference of the family doctor, a psychiatrist and the social or welfare worker to decide the proper disposal.

There is no justification for admitting an aged case of mental breakdown straight to a residential home.

More training about the problems of aging and of mental health should be given to medical and nursing students and refresher courses should be provided for the practitioners concerned. The general public should be better informed about the present favourable outcome in many forms of mental illness.

Allen Daley

Vital Statistics and Epidemiology

ALISON, F. & CORONE (Mme.). La mortalité des enfants agés de 1 à 14 ans et la mortalité des adolescents de 15 à 19 ans (1955–1956–1957). **[Mortality of Children Aged 1 to 14 Years and Adolescents of 15 to 19 in France in 1955 to 1957]** *Bull. Inst. Nat. Hyg.* Paris. 1959, Mar.–Apr., v. 14, No. 2, 385–99, 4 graphs.

Compared with western European countries the mortality in France is high at ages 1–4, low at ages 5–9 and 10–14, and about average for ages 15–19. The death rates in these 4 age groups in 1955 were the lowest recorded. A further fall was recorded in 1956, except at ages 5–9, but in 1957 a small rise occurred in each age group, except 5–9, due mainly to the outbreak of influenza and the death rates in 1957 were above those recorded in 1955 except at ages 1–4 where the rate was 14 per 100,000 lower. The death rates per 100,000 in 1957 were 166 at ages 1–4, 43·1 at ages 5–9, 43·7 at 10–14 and 81·3 at 15–19.

The deaths have been tabulated for 24 main causes. Accidents were the most important cause of death in these age groups, the rates compare favourably with those of several other western European countries and with the United States of America. Road transport accidents and drowning were the chief causes of accidental death among school children and young adults. Among the pre-school children burns were an additional important source of accidental death. The second largest cause of death at ages 1–14 was pneumonia and bronchopneumonia with a death-rate of 5·6 per 100,000. The death rate from infectious diseases was low and showed little variation in the 3 years, although diphtheria declined from 1·1 per 100,000 at ages 1–4 in 1955 to 0·5 in 1957 and at ages 5–9 from 0·5 to 0·3. The death rate from tuberculous meningitis at ages 1–4 decreased from 5·3 in 1955 to 3·2 in 1957 and other forms of tuberculosis fell from 1·5 to 1·0. Cancer and leukaemia were important causes of death in each age group and the mortality tended to rise during the 3 years. The death rate per 100,000 at ages 1–14 in 1957 was 4·2 for leukaemia and 3·3 for cancer and the male rate was about 25% above the female rate. At ages 1–4 in 1957 the death rate for pneumonia and bronchopneumonia was 15·4 per 100,000 and the death rate from congenital malformations was 9·2.

W. J. Martin

ALISON, F. & CORONE (Mme.). Mortalité foeto-infantile en 1957 (année entière). **[Stillbirth and Infant Mortality Rates in France in 1957]** *Bull. Inst. Nat. Hyg.* Paris. 1959, May–June, v. 14, No. 3, 597–610, 7 maps.

In France the infant mortality rate fell from 31·6 per 1,000 live births in 1956 to 29·2 in 1957 but the stillbirth rate rose slightly from 22·7 to 22·8 per 1,000 total births.

A considerable variation occurred between the rates of the *départements*: Corsica had the lowest stillbirth rate of 15 but the highest infant mortality of 48. This phenomenon of a low stillbirth rate and a high infant mortality was shown by several *départements*. It should be noted that under the system of registration employed, deaths of infants which occur before registration of birth are counted as stillbirths. The infant mortality was very high in some of the northern *départements*: a rate of 46 was recorded in the Pas-de-Calais, 41 in the Nord, 40 in the Somme but the Seine had the low rate of 22. In 1957 31 of the 90 *départements* had a stillbirth rate lower than the mean of 1954–56 while 79 *départements* had a lower infant mortality.

The percentage of infant deaths occurring in the first month of life in 1957 was 51·5 compared with 50·2 in 1956, or a rate per 1,000 live births of 15·0 against 15·8. The causes of infant deaths are tabulated under 22 headings. The greatest numbers in 1957 were due to prematurity with a rate per 1,000 of 5·4, congenital malformations 3·6, and toxicosis 2·9.

W. J. Martin

CANDIOTTI & MOINE, M. Aspect social de la France en fonction de sa mortalité et de sa natalité. **[Social Aspects of Death Rates and Birth Rates in France]** *Bull. Inst. Nat. Hyg.* Paris. May–June, v. 14, No. 3, 685–702.

The crude death rate in France is now less than 60% of the rate at the beginning of the century. The females have had a lower death rate throughout the period but the sex ratio of the death rates has been practically constant. As in other countries the greatest fall in the death rates has been in childhood, due to the large decrease in infectious diseases, and the

lowest fall in old age. As a result of the decrease in mortality the expectation of life at birth rose between 1861–65 and 1955–57 from 39 to 65 years for males and from 41 to 71 years for females. At age 60 the expectation of life has increased from 14 to 17 years for males and from 14 to 20 years for females.

The mortality from tuberculosis has declined continuously in recent years and has almost disappeared as a cause of death at ages 1–19 years. The crude death rate per 100,000 from tuberculosis in 1928 was 162 for males and 122 for females and in 1957 the rates were 37 and 13 respectively. The crude death rate from cancer has risen between 1928 and 1957 from 88 to 194 per 100,000 for males and from 104 to 174 for females. The increase in the cancer death rates affected all ages, the largest rise being in old age, but although the actual increases were small the relative increases were large in each age-group below 25 years. In 1957 the death rate from cerebro-vascular lesions, heart diseases, and vascular diseases were, respectively, 129, 218 and 37 for males and 147, 212, and 35 for females. Mortality from alcoholism showed a rise in 1957 compared with 1955, the death rate for males was 21 per 100,000 compared with 16 and for females the rate rose from 5 to 6; the death rate from cirrhosis of the liver rose from 34 to 42 for males but fell from 22 to 20 for females. The death rate from accidents has risen steadily in the last few years, the male rate rose from 72 per 100,000 in 1950 to 87 in 1957 and the female rate rose from 29 to 42 in the same period. The death rate from road accidents in 1957 was 31 per 100,000 for males and 7 for females.

The authors discuss the social and medical aspects of the current trend of the death rates in France.

W. J. Martin

DABB, R. G. **Deaths among African Children.** *Central African J. of Med.* 1959, Apr., v. 5, No. 4, 178–80.

Women attending the ante-natal clinic of the Mission Hospital at Blantyre, Nyasaland, were questioned about the deaths of their children and their standard of education. Details were obtained from 1,535 women who had 3,685 pregnancies, including stillbirths. The still-birth rate among these children was 50 per 1,000 births and the infant mortality was 242 per 1,000 live births. One-half of the women had received no education and 18% had had 4 years or more at school. There was a progression between education and infant survival. The percentage of children living rose from 51 for women with no education to 77 for the women who had spent 7 or more years at school. Abortions showed a similar trend, the rate was 10% for women with no schooling and 5% for the women with the longest period at school. The uneducated women had more children than the educated, the percentage of those with only 1 child being 17 among the women with no education and 32 for the women with the longest time at school. Expressed as a percentage of all deaths the chief causes of infant deaths were prematurity (30%), "fever" (19%), cough (including pneumonia) (13%), and diarrohea (10%).

[The author gives ages at death, but no comparisons can be made since it is obvious that the periods for which the children were exposed to risk varied considerably; the actual numbers surviving each age period are not given, so that an age-specific death rate cannot be found.]

W. J. Martin

GARDINER, C. E. **Maori Infant Mortality.** *New Zealand Med. J.* 1959, June, v. 58, No. 325, 321–40.

The Maori infant mortality has been high since records have been kept. In 1938 it was 153 per 1,000 live births falling to 54 in 1958; for the same period the European infant mortality fell from 36 to 19. The percentage fall for the past 20 years was 33·2 for European and 15·6 for Maori neonatal mortality and 37·7 for European and 52·9 for Maori postnatal infant mortality. For the quinquennium 1954–8 the Maori neonatal rate was 50% larger than the European rate and for the age group 1–12 months the Maori death-rate was nearly 7 times larger than the European. The Maori infants experience a higher death-rate for each cause of death than the European infants, the largest differences being due to respiratory and intestinal diseases. In 1958 the death-rate per 1,000 live births from influenza, pneumonia and bronchitis was 15·6 for the Maori and 2·1 for the European babies and for gastro-enteritis and diarrhoea the Maori rate was 6·1 and 0·2 for the Europeans.

A special survey was made to study the possible environmental factors influencing the high Maori mortality, in the Whangarei, Auckland, Hamilton and Gisborne, and the Palmerston North Health Districts. The survey included all Maori infants dying between the end of June 1954 and the beginning of July 1955 and these were compared with a sample of all Maori children and a sample of European children born during this period. The numbers studied in each group were 142, 196 and 129, respectively. In general the conditions were most unfavourable for the group of Maori infant deaths and most favourable for the Europeans with the other Maori group in an intermediate position. The Maori women have their children at younger ages and have more children than the Europeans, by ages 30–35 the Maori mothers have had an average of 5·9 children against 2·5 for the Europeans. The Europeans had more ante-natal consultations than the Maori and more were delivered in hospital, 99·2% compared with 80·5% for the Maori. The group of infants deaths had more complicated deliveries than the other two which were similar but the incidence of instrumental and surgical deliveries was 21% in the European group compared with 3% in the 2 Maori groups. Maori mothers had more illness within 6 weeks of delivery than the European mothers. The proportion who had a postnatal examination by a doctor was only one-half of that of the European women, and they had less advice on infant welfare.

On the average the Maori population lived in worse surroundings than the European, in older buildings in less accessible sites which were in rather worse situations, in less well built houses with more limited floor space and fewer rooms and consequently were often

overcrowded. The conditions of water supply, bath facilities, sanitation, refuse disposal, etc., were much better in the European than in the Maori dwellings.

W. J. Martin

PADLEY, R. **Cause-of-Death Statements in Ceylon. A Study in Levels of Diagnostic Reporting.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 4, 677–95. [13 refs.]

The difficulties in analysing data relating to cause of death in Ceylon arise from several causes. The system of registration is different in the 3 areas of the country, urban, estates and rural. In most urban areas the majority of deaths are classified by a medical practitioner but the completion of the death certificate often leaves something to be desired because of the single line cause of death and the lack of appreciation of the problems involved in attributing causes to death. On estates the responsibility of reporting deaths to the nearest medical officer is the superintendents'. In rural areas the registration is in the hand of the lay registrar and no medical certificate is customarily produced although the patient may have been attended by a medical practitioner in the last illness. Unfortunately the 3 types of registration districts are not mutually exclusive and some estates overlap into the urban area. In the rural areas the registrar is only literate in his own language and the lay diagnosis in many cases is descriptive of symptoms and may be related to conditions wholly unconnected with the disease which caused death. Attempts to translate and code these descriptions present considerable difficulties. Several of the important causes of death including typhoid, paratyphoid, meningococcal infections, pneumonia, appendicitis, cirrhosis of the liver, nephritis, congenital malformations, birth injuries, have no Sinhala term and consequently do not appear as a cause of death although such deaths are known to occur.

The author suggests ways by which improvement in registration in the present system could be attempted. A revision of the translation of Sinhala terms would help. Instruction should be given to lay registrars in selecting which symptoms should be reported as a result of their questioning the relative notifying the death. The elimination of the obscure Sinhala terms and their replacement by more precise diagnosis will take a skilled staff a long time to accomplish.

W. J. Martin

SPICER, C. C. & LIPTON, S. **Numerical Studies on some Contagious Distributions.** *J. Hygiene.* 1958, Dec., v. 56, No. 4, 516–22, 3 figs. [11 refs.]

This paper is an interesting assessment of the use of an electronic computer in the study of theoretical epidemiology. 3 mathematical models of the distribution of infection in small closed groups due respectively to BAILEY, FROST and GREENWOOD [this *Bulletin*, 1931, v. 6, 801] have been tested by working out, with an electronic computer, the numerical consequences of their application in communities ranging up to 40 individuals in size and under different conditions of probability of transfer of infection.

In the Frost model of family or closed-community epidemics, the number of fresh cases in each successive wave of the epidemic depends on the risk of transfer and the number of infective sources to which each susceptible is exposed. Greenwood's model is similar but ignores the possibility that the presence of more than one infective source at a time increases the risk of any susceptible being infected. Diagrams are given to illustrate the results of applying these models in different community conditions. The total epidemic size is, for equal possibility of infection, clearly greater for the first model.

Bailey's model of epidemic behaviour assumes that the infectiveness of a case is a continuous process and that the size of the completed epidemic depends on the ratio of the probability of a case being infectious to the rate at which such cases are effectively removed from circulation. The results with this continuous infection model are quite similar to those given by the other formulations. The authors conclude that, in conditions where any of these models may be reasonably expected to apply, a moderately infectious disease is likely to spread to almost all susceptible members in communities of 10 or more.

D. D. Reid

Communicable Diseases

For the bacteriology of these diseases see the section on Bacteriology below. For those communicable diseases conventionally regarded as tropical, readers are referred to the TROPICAL DISEASES BULLETIN

INFECTIVE DISEASES

In this section the abstracts are arranged as far as possible in the following order: General; Hospital Cross Infection; Diphtheria, Whooping Cough, Streptococcal Infections, Measles, Mumps; Chickenpox, Smallpox; Influenza and other Respiratory Virus Infections, Pneumonia; Hepatitis, Mononucleosis; Meningitis, Poliomyelitis and other Enteric Virus Infections; Arthropod-borne Virus Infections; Enteric Fevers.

RANKING, D. L. **Antibiotic-Resistant Staphylococcal Disease: an Obstetric, Surgical, Paediatric and Hospital Administrative Problem.** *South African Med. J.* 1959, June 27, v. 33, No. 26, 529–33, 1 fig. [15 refs.]

After an outbreak of staphylococcal sepsis in a hospital in Pietermaritzburg, Natal, the level of bacterial contamination of the hospital environment was investigated by means of air counts and blanket sweep counts.

Total air counts at the beginning of the 15-month investigation ranged from 53 to 286 organisms per cu. ft. in the theatre unit, 15 to 143 organisms in the obstetric unit and 115 to 178 in the surgical wards; the organisms included in some cases haemolytic streptococci and coagulase-positive staphylococci: the staphylococci were isolated only once, and the strain was resistent to several antibiotics. The blankets contained mostly bacteria associated with normal air pollution, but staphylococci, haemolytic streptococci and *Proteus* (once) were isolated from different samples.

Closing of a main corridor which bisected the theatre unit to general traffic and the use of an antiseptic spray reduced the counts 10-fold. Correction of the outflow, the institution of clean cotton clothes for theatre staff and cotton blankets for theatre patients further reduced counts to an acceptable level of 1–4 organisms/cu. ft.

Air counts in surgical wards fell 10-fold after more frequent laundering of blankets in Cirrasol and formalin treatment of blankets every 2 weeks, and damp dusting of the ward.

During the investigation there were 3 deaths of premature babies from a condition suggesting acute staphylococcal infection. A staphylococcus phage-type 80 was present in the hand lesion of a midwife and coagulase-positive staphylococci were isolated from the stool of one infant who died, and from incubators and clean linen. No more cases occurred after the cleaning of the nurseries, reduction of the number of beds and the use of autoclaved linen in the incubators.

The number of cases of staphylococcal sepsis (due to organisms of the same multiply-resistant antibiotic pattern) is given for the second-half of the period of study [there is no indication, however, of the number of patients at risk] and it was decided to convert one ward into an isolation ward. *M. Patricia Jevons*

WEINSTEIN, H. J. **The Relation between the Nasal-Staphylococcal-Carrier State and the Incidence of Postoperative Complications.** *New England J. of Med.* 1959, June, 25, v. 260, No. 26, 1303–8. [12 refs.]

Nasal cultures were taken from patients scheduled for surgical operation in a chest unit. 43 of 125 were found to carry *Staphylococcus aureus*. Some of these patients were given bacitracin-neomycin ointment to their anterior nares 3 times a day for 4 days before and 4–5 days after operation.

Any "untoward manifestation that prevented an 'ideal' postoperative course" was called a complication. 43% of the nasal carriers, and only 26% of the non-carriers had complications. In fact only 35 of the carriers and 66 of the non-carriers had operations; the former had 15 and the latter 8 infected complications, which were pneumonia, wound infection, and empyema. *Staph. aureus* was responsible for 15 of the complications in the carriers but only 3 of those in the non-carriers. A variety of phage types were involved. The nasal antibiotic appeared to have no value. *R. E. O. Williams*

WEINSTEIN, H. J. **Control of Nasal-Staphylococcal-Carrier States.** *New England J. of Med.* 1959, June 25, v. 260, No. 26, 1308–10. [11 refs.]

606 nasal cultures from 110 members of a hospital staff were examined for *Staphylococcus aureus* and 39% were positive. The nasal carriers were included in a controlled trial of the effect of local application of a bacitracin-neomycin ointment to the anterior nares 3 times daily for 7 days. Repeat cultures were examined before and 1 week after the treatment course. Control subjects had a placebo ointment. 72% of 39 test subjects who had a positive culture before treatment had a negative culture afterwards, compared with 23% of 22 carriers given the placebo and 22% of 37 given no treatment. [No later follow-up is reported.] *R. E. O. Williams*

SEVER, J. L. **Possible Role of Humidifying Equipment in Spread of Infections from the Newborn Nursery.** *Pediatrics.* Springfield, Ill. 1959, July, v. 24, No. 1, 50–53.

Bacteriological studies made of the water in the humidifying devices of 14 infants' incubators revealed total bacterial counts between 850 and 14,850 per ml. Coliform bacilli predominated but coagulase-positive staphylococci were also found. Regular cleansing of

the apparatus was instituted and sterile distilled water was used. Tests made after these changes revealed 20–125 colonies per ml. *R. E. O. Williams*

OCKLITZ, H. W. & ROMEIKAT, I. Die Verhütung der Schmierinfektion in der Schwesternarbeit auf der Säuglingsstation. [**The Prevention of Contact Infection in the Nursing Procedures in a Maternity Hospital Ward**] *Arch. f. Hyg. u. Bakt.* 1959, Apr., v. 143, No. 3, 172–91, 4 figs.

140 cultures taken from various objects in a maternity hospital ward revealed pathogenic *Escherichia coli* in 3 cases and *Staphylococcus aureus* in 7. The possibility of contact spread of these organisms was therefore evident. An analysis was made of the work done by the nursing and ancillary staff; the various "faults" observed in their technique are listed in detail together with the methods recommended for avoiding them. The lists are very comprehensive but the faults and methods do not differ in essentials from those found and recommended elsewhere. *R. E. O. Williams*

LEVINE, L. & WYMAN, Louise. **Factors affecting the Efficiency of Combined Prophylactics: Effect of Poliomyelitis Vaccine on Diphtheria Toxoid.** *J. Immunology.* 1957, Aug., v. 79, No. 2, 89–93.

"A study of the effect upon the primary and secondary immunizing efficiency of diphtheria toxoid for guinea pigs, after admixing varying concentrations of poliomyelitis vaccine, was presented. No significant effect on the response of the animals to the toxoid, due to the vaccine, could be demonstrated."

TISHCHENKO, I. T. & PRIMAK, D. O. **Epidemiological Importance of Scarlet Fever Patients treated at Home, and Secondary Complications occurring in Such Patients.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 6, 900–903. [Translated from Russian.]

In Russia an order was made in July 1955 for the abolition of compulsory hospitalization for scarlet fever, and the extension of indications for treating patients at home. As a result the percentage of such patients treated at home increased from 3·4% in 1955 to 49% in the first quarter of 1957. The result has been very satisfactory, at least in the Kiev district where over 99% of the cases are classified as mild or of average severity. Enquiries have now shown that the number of secondary cases in home contacts is negligible, and that the number of complications in patients treated at home is about one-half of that occurring in hospitals, probably owing to absence of exposure to infection from other patients. It is concluded that the question whether to hospitalize scarlet fever patients or to leave them at home should be decided by the epidemiologist and the local paediatrician. [The treatment of scarlet fever at home has been generally practised, in Britain at least, for 10 years or more.] *H. Stanley Banks*

MARKHAM, N. P. **Streptococcal Infections.** *New Zealand Med. J.* 1959, Apr., v. 58, No. 324, 179–83, 1 fig.

This paper reviews the β-haemolytic streptococcal infections recognized in material coming to a laboratory in Dunedin N.Z. from April 1956 to March 1958. 417 group A strains were isolated from lesions, with a striking rise in frequency in 1957–8; most (204) came from skin lesions, often also infected with staphylococci. Of 118 strains not belonging to group A, 57 were group B, coming predominantly from the female genital tract. *R. E. O. Williams*

SASLAW, M. S. & STREITFELD, M. M. **Recovery of β Hemolytic Streptococci from Throats of Mother and Child: Relationship to Respiratory Illness.** *J. Infect. Dis.* 1959, May–June, v. 104, No. 3, 233–7.

Throat swabs were taken weekly and blood samples monthly, from 53 children at a school in Miami, Fla. during the 8-month period October 1956–May 1957; similar samples were taken, rather less regularly, from the mothers of 36. 6 children who were absent from school for respiratory illness had group A streptococci at the time, but in only 2 had these organisms been present for less than 1 week; only 2 (including 1 of the 2 with recent infection) had a significant rise in antistreptolysin. Streptococci of 1 Lancefield group were recovered from mother and child simultaneously on only 5 occasions. *R. E. O. Williams*

ESMANN, V. **Streptococcal and Non-Streptococcal Sore Throat.** *Acta Med. Scandinavica.* 1959, Mar. 23, v. 163, No. 4, 265–76, 2 figs. [35 refs.]

This is an attempt to find distinguishing characteristics between streptococcal and non-streptococcal sore throat. 81 patients aged 8 to 60 (two-thirds being under 30), referred to a hospital in Denmark by 20 general practitioners for treatment of sore throat during a 6-month period December to May, were submitted to detailed clinical and laboratory examinations. The sore throat was found to be due to streptococci in 42%, to adenovirus in 5%, to mononucleosis in 7%, to Vincent's disease in 2%, and the cause was undetermined in 44%. Except for redness of the fauces, which was absent in most cases of non-streptococcal origin, the clinical observations were inconclusive as to aetiology, but pharyngeal cultures for β-haemolytic streptococci were of high value when the growth of streptococci was profuse. An increase of anti-streptolysin titre of 100% between the acute and convalescent stages, with a final titre over 100, was found to be a significant sign of streptococcal sore throat, as was also an increase in titre of anti-streptococcal hyaluronidase, with a final titre exceeding 9,000. One or both of these tests was positive in this sense in 62% of the patients, with streptococcal sore throat.
H. Stanley Banks

JUROW, H. N. & CLARK, Rosemary. **Erysipelas in Pregnancy. Report of a Case with Fatal Outcome.** *J. Amer. Med. Ass.* 1959, July 11, v. 170, No. 11, 1299–302, 2 figs. [12 refs.]

This is a record of a fatal case of erysipelas in a pregnant woman aged 32. The condition started as an insect bite on the face and was at first treated with antihistamines. When no improvement occurred, corticosteroids were added to the treatment. She was first treated with an antibiotic, chlortetracycline, 9 days after the first appearance of the lesion: by then the oedema had spread over face, chin and neck. Smears from bullae showed haemolytic streptococci sensitive to penicillin, tetracycline and streptomycin. The lesion continued to advance down the chest wall and haemorrhagic bullae appeared. The patient gave birth to a healthy infant but shortly afterwards developed dyspnoea, collapsed and died. Autopsy showed inflammation of the subcutaneous tissues of neck and chest, of the areolar and lymphoid tissues of the mediastinum, the external surface of the pericardium, the thymus gland and the pleurae. *A. B. Christie*

VALLE, J. R. & TEIXEIRA, I. Tratamento da coqueluche pela terramicina intramuscular. [**Treatment of Whooping Cough with Intramuscular Oxytetracycline**] *Bol. Centro Estudos Hosp. Servidores Estado.* Rio de Janeiro. 1959, June, v. 11, No. 6, 233–8, 1 fig.

The English summary appended to the paper is as follows:—

"Intramuscular Terramycin was administered to a series of 16 acute uncomplicated cases of whooping cough, according to the following method:

"1) Children were treated at home checked by their parents, who were instructed to fill out a special chart.

"2) After a 24 hour observation without any treatment whatsoever, Terramycin was started on.

"3) Treatment consisted of 5 mg. per kilo of body weight, per day, of intramuscular Terramycin, divided into two injections at 12 hourly intervals, for 10 days.

"4) No cough sedative was used: Terramycin alone was given.

Results.

"1) Early intramuscular Terramycin for treatment of whooping cough in its acute stage, showed to be of great therapeutic value on our series of cases.

"2) Effectiveness was observed to occur mainly on decreasing or on disappearance of vomiting and whoopings. Also a decrease in rate and lessening of paroxysms was obtained.

"3) All the cases but one, improved.

"4) No untoward effects were observed and injections were well tolerated."

CROSS, R. M. **Vaccination Technique and the Control of Smallpox Epidemics.** *Lancet.* 1959, May 23, 1092–3, 4 figs.

Cross shows in this paper that the rate at which immunity to vaccinia virus develops after primary vaccination is related to the size of the vesicular reaction. This, in turn, depends both on the potency of the vaccine and on the number of susceptible dermal cells initially involved in the vaccination. A potent vaccine applied by ¼ inch scratch may be expected to give rise to measurable circulating antibodies in the majority of subjects by about 2 weeks after vaccination. A very small vesicle resulting from a short scratch or a deteriorated vaccine will probably not lead to much antibody production in 2 weeks, but by 3 weeks after vaccination, protection—judged by response to challenge vaccination and by antibody levels—is indistinguishable whatever the size of the initial stimulus.

The importance is stressed of the need for *adequate* successful vaccination to confer protection against smallpox as early as possible. *Colin Kaplan*

SEMPLE, A. B., PARRY, W. H. & HOBDAY, T. L. **Anti-vaccinial Gamma-Globulin. A Further Report on Smallpox Prophylaxis.** *Lancet.* 1959, July 11, 34.

In March 1959 a medical student in Liverpool developed an attack of smallpox. The source of the infection was not determined. The nature of the virus was confirmed "by laboratory tests" and was regarded as that of variola major [though how the distinction from variola minor was arrived at is not stated]. The patient, who had been vaccinated 20 years earlier, recovered.

4 close contacts were at special risk: these had been vaccinated 45 years ago, 43 years ago, 57 years ago with re-vaccination 36 years ago, and 49 years ago with re-vaccination 17 years ago. [Results or evidence of these reputed vaccinations are not given.] All were now revaccinated, but at least 5 days after first exposure to smallpox infection. In addition, each received 1·5 gm. of antivaccinial gamma globulin 2 days (in one instance, 3 days) after revaccination. Primary takes followed in each case; and in no instance did any evidence of smallpox appear.

Another contact, "owing to recent revaccination" was not given gamma globulin, but was revaccinated [result not stated]. On 11th day after exposure to smallpox he became ill and a "prodromal rash" appeared on 13th day: a focal rash did not develop. [The authors appear to have accepted this as an "abortive" attack of smallpox, but, again, the evidence seems inconclusive. Assessment of the true value of gamma globulin in smallpox prophylaxis must await large-scale controlled trials in which, among other things, the vaccinial state of the subjects is accurately known. Meanwhile, active immunization must remain the sheet-anchor, and nothing should be done to hamper the prospects of a good vaccinial "take". The abstracter would not accept the view expressed by the authors of this article that in these cases "vaccination had been performed too late to ensure protection".] *J. Pickford Marsden*

FRY, J. **Influenza, 1959. The Story of an Epidemic.** *Brit. Med. J.* 1959, Aug. 8, 135–8, 1 graph.

This paper contains an excellent account by a general practitioner of a violent epidemic of influenza which occurred in January 1959 in Beckenham, Kent, from his own experience of the disease among his patients.

This experience is compared with that of influenza in 1957 and other years in the same practice which the author described in a previous paper in 1958 [this *Bulletin*, 1958 v. 33, 434].

A table sets out the age distribution of the 6,016 patients at risk in the practice. Among these there were 849 known cases of influenza during the 9-week period of the epidemic. The age distribution of the influenza patients is recorded in some detail. The highest incidence was in children and young adults—21% of those at risk at age 0–5 years, 26% at 5–10, 20% at 10–15 years and diminishing to 4% in the age-group 70 + years. It is noted that only 4% of the 849 patients seen in the 1959 epidemic had suffered from influenza in 1957. The clinical features are described. There were 80 patients (9·5%) who suffered from chest complications—7 with lobar pneumonia, 43 with segmental pneumonia and 30 with acute bronchitis. Treatment of most of the patients was with simple non-specific measures. Antibiotics were administered only to the 56 patients with complications who were severely or moderately ill.

Sputum examinations did not reveal any predominant organisms. Studies carried out on the sera of 20 patients showed that the epidemic was due to a mixture of influenza viruses A and B. *M. E. Delafield*

Melnotte, P. Données actuelles sur la grippe. Les enseignements de la pandémie de 1957–58. [**Findings in the Pandemic of Influenza in 1957–58**] *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1959, Apr.–May, v. 7, No. 3, 235–76. [34 refs.]

The first section of this article reviews the spread of the epidemic across the world and the incidence and mortality in various countries. In France the estimated attack rate was 20% and the deaths rose from 60 in September 1957 to 1,676 in October and 3,593 in November, and then fell to 2,606 in December, 1,028 in January and 618 in February. The mortality in November varied considerably between the different *départements* of the country, from 2 per 100,000 in Seine to 21 in Savoy.

The author discusses the clinical aspects and the complications found in the 1957 outbreak and suggests that the great difference between the mortality in 1918 and 1957 outbreaks was largely due to modern therapeutic agents acting on the secondary infections. The epidemiology of influenza is reviewed and the findings of other workers, the method of infection, the period of infectivity, the possible reservoirs of infection and other aspects of the course of the disease are discussed. Prophylaxis is studied in detail and the conclusions reached by various workers are compared. The composition and strength of the vaccines, the number and method of inoculations, the effect of adjuvants (aluminium phosphate and mineral oil), and the use of an emulsifier on the efficacy of the vaccine, are discussed and the results obtained in some trials are quoted. The manufacture of a vaccine and the inoculation of a large number of persons in a limited time present great difficulties and in France a list of priority classes was drawn up, but the rapidity of the epidemic prevented a completion of the programme.

The author concludes by emphasizing that influenza is still, despite the very low fatality rate of the 1957 epidemic, a frightening menace. *W. J. Martin*

Cocuzza, G. & Roccuzzo, M. Frequenza degli anticorpi verso il virus Sendai nella popolazione normale siciliana. [**Antibodies to Sendai Virus in the Normal Population of Sicily**] *Giorn. di Batteriol., Virol. ed Immunol.* 1959, Mar.–Apr., v. 52, Nos. 3–4, 114–20. [19 refs.] English summary (5 lines).

27% of 60 sera from persons aged 4 months to 39 years were positive for antibodies to Sendai virus. The youngest positive subject was aged 5 years, and most of the positive results were found in persons over 18. The infection seems to have been present for a long time. *Charles Wilcocks*

Grayston, J. T., Wang, San-Pin, & Pierce, W. E. **Recurrence of Asian Variant Influenza in the Far East. Report of 1958 Epidemic in Marine Corps on Okinawa.** *J. Amer. Med. Ass.* 1959, Feb. 7, v. 169, No. 6, 577–9.

An outbreak of influenza occurred in August 1958 involving 52 U.S. Marines on Okinawa. The three viruses isolated were closely related to the set of 1957 Asian variants of type A virus, and a sample of the men involved had a rise of titre of antibodies to the Asian variant in paired sera taken in the acute and convalescent stages respectively. Nearly all of these men had been vaccinated against the Asian variant within the preceding 9 months. The illness was mild with no complications.

It is suggested that since such an outbreak occurred in a well vaccinated population with an unusually high risk of exposure, another world-wide epidemic due to one of these variant strains is a possibility within the present year. *H. Stanley Banks*

Masi, A. T., Timothee, R., Janer, J. L. & Mariñelarena, R. Epidemia de influenza asiática en Puerto Rico. [**Asiatic Influenza Epidemic in Puerto Rico**] *Bol. Oficina Sanitaria Panamericana.* 1959, Apr., v. 46, No. 4, 313–24, 1 graph. [13 refs.]

Influenza was brought into Puerto Rico in July 1957 by a group of boy scouts who had attended a Jamboree in Valley Forge, Pennsylvania.

When the schools and colleges opened at the end of August (34th week of the year) absences due to illness were above the normal. Industry, also, reported a high sickness rate. The peak of new cases was in the 38th week. The total number of new cases of influenza notified during the 14 weeks ended November 29 was 117,111: the population of the island is 2,281,000. The case rate was slightly higher for females than for males specially in the age-group 5–44. During the 50 days when specific enquiry was made the excess absence from schools was 4·3% and in industry 3·9%.

The death-rate was not raised until the 38th week. The excess mortality was mainly in the age-groups over 65 and under 12 months though in neither of them

was the case incidence unduly high: 81% of the excess deaths were in these 2 extremes of life. The highest incidence of the disease was in the age-group 5–14 with 37·1% of the cases and 13·4% of male and 12·9% of the female population. The registered causes of the excess deaths in the aged were mainly from pneumonia and influenza but they, also, occurred from chronic diseases such as cardiovascular and tuberculosis but not from cancer, diabetes or nephritis. Among infants the excess was due to pneumonia and influenza and to pneumonia of the newly born.

Virus A/Jap-305 was grown from 10 out of the 19 patients whose throat swabs were examined. Complement-fixation tests made on the serum showed that antibodies were increased in all against Asiatic type virus; in 9 against A/Denver and in 3 against B/Grandes Lagos. Studies made of the serum of the 9 from whom virus was not isolated showed increased antibody content against Asiatic types. A table gives details of all these laboratory investigations.

A vaccine was not used and it is recommended that should influenza become pandemic vaccine should be available in priority for the age-groups with the highest mortality. *Allen Daley*

LACKMAN, D., CASEY, Mary, PHILIP, R., OWEN, Cora & REINHARD, K. **A Comparison of Influenza in the Northwestern United States caused by A-Prime and Asian Influenza Viruses.** *Canadian J. Pub. Health.* 1959, Feb., v. 50, No. 2, 71–9.

The immunological relationships of A-prime and Asian influenza viruses were studied in 2 large groups in which an outbreak of Asian influenza occurred in the autumn of 1957, which had been preceded by outbreaks of A-prime influenza in March 1956 and March 1957. No evidence was found of a lowered attack rate for Asian influenza because of pre-existing A-prime haemagglutinin-inhibition (HI) antibodies. The clinical findings in the Asian influenza outbreak were the more pronounced, but the duration of both illnesses was about the same—3–6 days.

Asian influenza vaccine, administered after the disease, had a strong booster effect on Asian HI antibodies, and some effect on A-prime HI antibodies. The clinical attack rates in groups with opportunities for close contact were above 40%, while in the district generally 30% of the population showed serological evidence of infection with the Asian virus.

H. Stanley Banks

OSEASOHN, R., ADELSON, L. & KAJI, M. **Clinicopathologic Study of Thirty-Three Fatal Cases of Asian Influenza.** *New England J. of Med.* 1959, Mar. 12, v. 260, No. 11, 509–18, 7 figs. [17 refs.]

33 fatal cases of Asian influenza in patients of all ages were studied in Cleveland, Ohio, between September 28 and December 17, 1957. The majority came under investigation through the coroner, because of sudden and unexplained death, or of the association of the death with the influenza epidemic. The study is particularly valuable because of the detailed pathological, bacteriological, and virological examination of fulminant cases of different types, such as combined viral and staphylococcal pneumonitis, abacterial influenzal pneumonitis, influenza with pneumococcal pneumonia and bacteraemia, and cases with encephalitic symptoms. Such types were more common in previously healthy and young persons, but the series includes a few older chronic sick persons in whom the attack of influenza brought about the fatal issue.

Post-mortem examination of the 4 cases with convulsions and coma following mild acute respiratory symptoms, disclosed only cerebral oedema and congestion with no histological evidence of encephalitis. It is felt that the designation "encephalopathy" is more appropriate than "encephalitis" to this type of case occurring during epidemics of influenza. The manner in which the central nervous system is involved remains unknown. In the lungs hyaline membrane, now regarded as a non-specific finding, was relatively more frequent in pneumococcal and abacterial than in staphylococcal cases. Myocarditis was present in almost one-third of the cases, but the virus was found only in 1 of 14 myocardial suspensions examined, and even then was confined to the arterioles. It is considered that the frequent occurrence of myocarditis in fulminant influenza may be associated with anoxia. [Myocarditis is, however, not an uncommon finding in deaths from acute viral disease, *e.g.* in smallpox and poliomyelitis.] *H. Stanley Banks*

MARTIN, C. M., KUNIN, C. M., GOTTLIEB, L. S., BARNES, Mildred W., LIU, C. & FINLAND, M. **Asian Influenza A in Boston, 1957–1958. I. Observations in Thirty-Two Influenza-Associated Fatal Cases.** *Arch. Intern. Med.* 1959, Apr., v. 103, No. 4, 515–31, 14 figs. [15 refs.]

MARTIN, C. M., KUNIN, C. M., GOTTLIEB, L. S. & FINLAND, M., with the technical assistance of Mildred W. BARNES, Clare WILCOX & Ann NAJARIAN. **II. Severe Staphylococcal Pneumonia Complicating Influenza.** *Ibid.*, 532–42. [25 refs.]

I. This is a thoroughly detailed study by FINLAND and his group of 32 fatal cases of Asian influenza, aged 11–71, in Boston and district. The clinical, laboratory and post-mortem findings were not unlike those of earlier influenza epidemics. A high percentage of the patients suffered from chronic heart disease or respiratory insufficiency, and there was an undue proportion of pregnant women.

Strains of influenza A virus were isolated from the tissues of 44% of the patients, and, by means of the fluorescein-labelled antibody technique, influenza A viral antigen was demonstrated in interstitial macrophages in the respiratory tract in 31%, but not in the heart even when diffuse myocarditis was present. It was not found possible to make a prompt diagnostic differentiation between pure influenzal pneumonia and post-influenzal bacterial pneumonia, except when a specific pathogen was revealed in the sputum, or cavitation seen in a chest film.

In order to save life in patients presenting with signs usually associated with fatal influenza, they

should be treated promptly as if they were proved staphylococcal pneumonias, until that diagnosis is disproved. The relative futility of standard supportive measures in preventing eventual asphyxia was demonstrated, and the need for the development of a practical "artificial lung" for such cases is emphasized.

II. The clinical and laboratory findings in 11 fatal and 9 non-fatal cases of staphylococcal pneumonia complicating Asian influenza in Boston and district are compared. The fatal cases were generally characterized by more severe and rapidly progressing illness, less accurate diagnosis, and relatively ineffective antibiotic therapy. A very high proportion of staphylococci found in influenza cases admitted from Boston and district were resistant to multiple antibiotics, and were of phage types usually associated with hospital-acquired infections. Disk sensitivity tests performed directly or sputum or body fluids containing staphylococci were a reliable guide for the selection of effective antibiotics. The antibiotic combination most often associated with survival was erythromycin and chloramphenicol, with or without novobiocin, but, in conditions so variable, the superiority of any one effective regimen over another cannot be asserted with certainty. During epidemic influenza, however, in areas where major staphylococcal infections are common, all patients with signs of potentially fatal influenza should be treated promptly as if they were cases of antibiotic-resistant staphylococcal pneumonia, until that diagnosis can be disproved. *H. Stanley Banks*

Cocuzza, G., Panella, I. & Mangiameli, S. Trasmissibilità transplacentare degli anticorpi antiinfluenzali. [**The Transmission of Influenza Antibodies through the Placenta**] *Giorn. di Batteriol., Virol. ed Immunol.* 1959, Mar.–Apr., v. 52, Nos. 3/4, 121–7. [19 refs.] English summary.

The passage to the foetus of antibodies against type A (PR 8 and Singapore 1–57 strains), type B (Lee strain), and type D (Sendai strain) was studied in 34 cases, by taking the maternal blood during labour or on the day after, and using cord blood. The haemagglutinin inhibition test was used.

Antibody levels were in most cases equal or differed only by one doubling-up dilution, except for antibodies against the Singapore strain which were found to be more than 4 times more abundant in the mother in 7 cases out of 13. The authors conclude that antibodies in cases of recent infection by the Singapore strain get through the placental barrier with greater difficulty than other influenzal antibodies.

E. Agius

Rendtorff, R. C., Walker, Lillie C., Rowland, M. Eloise & Packer, H. **Intradermal Immunization against Asian Influenza in Children.** *J. Amer. Med. Ass.* 1959, May 30, v. 170, No. 5, 524–8. [13 refs.]

Efficacy of vaccination against influenza by a monovalent vaccine administered by the intradermal route was studied during an outbreak of Asian influenza among 168 orphanage children from 1 to 17 years old. Each child was given 2 doses (0·1 ml.) of a vaccine containing 200 chicken-cell agglutinating units of Asian influenza virus per ml. Results of both clinical and serological studies suggest that a considerable degree of protection was conferred by vaccination.

H. G. Pereira

Rapmund, G., Johnson, R. T., Bankhead, Annie S., Herman, Y. F. & Dandridge, O. W. **The Diagnosis of Asian Influenza Virus Infection after Recent Immunization.** *U.S. Armed Forces Med. J.* 1959, June, v. 10, No. 6, 637–49. [14 refs.]

The value of different techniques used for the laboratory diagnosis of influenza was investigated during the early stages of the 1957 epidemic. Patients were divided into 3 groups, the first consisting of 11 unvaccinated patients, the second of 11 patients vaccinated against Asian influenza virus 21 or more days before their illness and the third of 20 patients similarly vaccinated from 4 to 19 days before their illness. All patients had a clinical diagnosis of influenza and no difference in clinical picture was observed between the unvaccinated and vaccinated groups. Serological diagnosis based on 4-fold greater rises in complement-fixing or haemagglutination-inhibition antibodies was highly successful in the first group, less so in the second group and gave poor results in the third group, for which the majority of diagnoses had to be based on virus isolation.

The possible reasons for this failure of serological tests in the diagnosis of influenza in recently vaccinated subjects are discussed. *H. G. Pereira*

Beam, W. E., Jr., Grayston, J. T. & Watten, R. H. **Second Asian Influenza Epidemics occurring in Vaccinated Men Aboard U.S. Navy Vessels.** *J. Infect. Dis.* 1959, July–Aug., v. 105, No. 1, 38–44. [12 refs.]

This paper, from the United States Naval Medical Research Unit No. 2 and the Department of Medicine, University of Chicago School of Medicine, contains a detailed report on second epidemics of Asian influenza which occurred on U.S. Navy vessels visiting Japanese ports in November 1957. The 1957 influenza pandemic had begun in February on the mainland of China. "These outbreaks are of additional interest since most of the men involved had received vaccine containing the Asian variant strain."

A full description is given of the methods used in the collection of specimens and the virus studies carried out, the epidemiological history, the clinical disease and the results of serological tests.

Each of the 5 ships, an aircraft carrier and 4 destroyers, had had previous experience with influenza-like illness between June 30 and July 14, 1957 while in ports in southern California. The aircraft carrier had 184 admissions to sickbay and an unrecorded number of men confined to quarters. A few serological tests suggested that the epidemic was Asian influenza. During August and September routine immunization with polyvalent influenza vaccine was carried out. On October 14 additional immunization was performed

with a special 1957 vaccine "containing 200 CCA units per ml of the Jap 305 Asian variant strain along with a similar amount of swine, PR-301, FM-1 and 1954 Great Lakes B strains". The second influenza epidemic on the carrier began suddenly on November 4, 1957, with 137 cases in the first 3 days and ended about November 27 by which time a total of 447 cases had been diagnosed. "The over-all attack rate was approximately 16%." In 1 of the destroyers the attack rate was 50%.

There is a good discussion in which there is particular reference to the "high percentage of Asian strain virus isolations from the clinical specimens" which "was undoubtedly due to careful handling and prompt freezing". The second outbreaks occurred among the men who escaped clinical disease during the first epidemic. The vaccine administered failed to prevent the extensive second epidemics yet "it cannot be stated that the Asian variant vaccine had no effect since no control study was performed". *M. E. Delafield*

VARGOSKO, A. J., CHANOCK, R. M., HUEBNER, R. J., LUCKEY, Alia H., KIM, H. W., CUMMING, Christine & PARROTT, R. H. **Association of Type 2 Hemadsorption (Parainfluenza 1) Virus and Asian Influenza A Virus with Infectious Croup.** *New England J. of Med.* 1959, July 2, v. 261, No. 1, 1–9. [13 refs.]

Virus isolation and serological tests carried out on 47 children admitted to hospital with a diagnosis of infectious croup gave evidence of infection by type 2 haemadsorption virus (parainfluenza 1) in 36% of patients, by Asian influenza virus in 19% and by adenovirus, croup-associated virus or type 1 haemadsorption virus (parainfluenza 3) in 9%. The frequencies of virus infection detected by similar laboratory tests among 949 children of comparable age but free from clinical signs of respiratory or other infections were of 0·4% for type 2 haemadsorption virus, 0·2% for Asian influenza virus and 1·6% for type 1 haemadsorption virus, croup-associated virus or adenovirus. No pathogenic bacteria (beta-haemolytic streptococcus, *Haemophilus influenzae*, pneumococcus or coagulase-positive haemolytic staphylococcus) were present in throat swabs from 22 of 36 children with croup tested and bacteria were equally frequent among patients with or without evidence of virus infection. The clinical picture of infectious croup associated with Asian influenza virus or not associated with known virus infection did not differ significantly from that observed among patients infected with type 2 haemadsorption virus.

[See also this *Bulletin*, 1959, v. 34, 730.]

H. G. Pereira

MACDOUGALL, Lorna G. & BEECHER, J. L. **Pneumonia in African Children. A Clinical, Bacteriological and Radiological Study.** *East African Med. J.* 1959, Jan., v. 36, No. 1, 36–43.

This study was in 80 consecutive patients with an age range of 1 month to 9 years, admitted to hospital in Nairobi with presenting symptoms and signs of acute respiratory infection. The majority were cases of acute lobar pneumonia or bronchopneumonia, but 7 had a primary pyogenic respiratory infection, and 7 were found to be suffering from tuberculosis, typhoid, measles, or whooping cough—infections which should not be admitted to an open ward.

All but 8 were treated with penicillin, but a clinical response was obtained only in 58%, and there were 7 deaths, all under 2 years of age, a death-rate of 8·7%. A variety of pathogenic bacteria was isolated on retropharyngeal swabs, mainly *Streptococcus pneumoniae* and *Staphylococcus aureus*; 88% of these organisms were sensitive to chloramphenicol and streptomycin, and only 45% to penicillin.

The relative failure of penicillin as a routine treatment of pneumonia in these African children was probably due to the widespread use of penicillin and sulphonamides in the out-patient dispensaries in the district. Penicillin was found to be effective as a rule only when there was a marked clinical response within 24–48 hours. The radiological picture sometimes gives a clue to the probable causative organism but no consistent correlation was found. The treatment of each case must therefore be decided on its merits. If penicillin fails, chloramphenicol is probably the next choice, unless tuberculosis cannot be definitely excluded, when streptomycin alone may be appropriate.

H. Stanley Banks

WHITTAKER, L. R. **The Radiological Diagnosis of the Acute Pneumonia in Children. A Preliminary Report.** *East African Med. J.* 1959, Apr., v. 36, No. 4, 200–208, 4 figs. [18 refs.]

This is a preliminary report on the radiological diagnosis of pneumonia, with reference to the possibility of identifying the type of pathological process under development in the lungs, and the probable organism causing that particular process, *e.g.* predominant bronchial involvement in influenzal pneumonia, and abscess formation in staphylococcal pneumonia. The 4 figures illustrate the distinctive radiological patterns that may be present in pneumococcal, streptococcal, influenzal, and staphylococcal pneumonia respectively. For success in radiological diagnosis of this exceptional degree, the radiographs must be of good quality and be taken early in the disease, and a lateral as well as a postero-anterior view must be taken in each case, with the affected side, if possible, nearer to the film in the lateral view. A further report on a large series is promised. [A praiseworthy attempt to advance the subject of radiological diagnosis.] *H. Stanley Banks*

EDE, S., DAVIS, G. M. & HOLMES, F. H. **Staphylococcic Pneumonia.** *J. Amer. Med. Ass.* 1959, June 6, v. 170, No. 6, 638–43, 6 figs.

This is a description of staphylococcal pneumonia based on 36 cases seen in the last 3 years in naval personnel in a U.S. Naval Hospital. Only 1 death occurred—a very different experience from that frequently encountered in a run of general civilian cases of all ages and with a high proportion of pre-existing chronic heart and respiratory disease. 34 of the cases were primary infections, and only 2 were secondary

to observed staphylococcal foci. All but 4 of the cases were apparently unconnected with hospital staff or patients. The good results obtained in the severer cases are attributed to the use of a combination of chloramphenicol and erythromycin, or of novobiocin and erythromycin.

There was a high proportion of pleural and other complications. Early surgical intervention is recommended, particularly by means of closed under-water tube drainage; a *large* catheter is inserted into the pleural space by open operation down to the intercostal muscle, and is connected up to a drainage system consisting of two bottles and a pump. This device can be very effective if applied early in pyopneumothorax, empyeme, or progressive pleural effusion.

An attempt is made to show that staphylococcal pneumonia, contrary to current opinion, has not increased in incidence since the introduction of antibiotics. [This may well be so, although the evidence adduced would be unlikely to satisfy a statistician.]

H. Stanley Banks

Leng-Levy, J., David-Chausse, J., Gibaud, P. & Battin, J. Le traitement des pleuro-pneumopathies aiguës par un sulfamide nouveau à action prolongée: le Ro 4–0517. **[The Treatment of Acute Pneumonia with a New Long-acting Sulphonamide, Ro 4–0517]** *J. Méd. de Bordeaux.* 1959, June, v. 136, No. 6, 713–20, 3 charts & 4 figs. on 2 pls.

Ro 4–0517 is a long-acting sulphonamide the formula of which is not given in this article. Given to adults in a dose of 4 tablets the first day, maximum concentration in the plasma is obtained in 20 hours and is maintained by a dose of 1 tablet twice daily. In treating a series of 32 patients suffering from acute pneumonia, 19 of whom received only Ro 4–0517, the authors found the clinical and radiological results excellent. Tolerance was perfect, there being no side effects or alteration of blood picture. The authors regard it as the equal of antibiotics in efficacy.

A. B. Christie

Stuart-Harris, C. H. **Chemotherapy of Non-Tuberculous Pulmonary Infections.** *Brit. Med. J.* 1959, June 27, 1606–10. [31 refs.]

After pointing out that the clinical picture of pneumonias has changed during the past 20 years the author is not convinced that this is wholly due to modern drug treatment. He describes the treatment of various acute infections of the lungs and bronchi.

For bacterial pneumonia the safety of penicillin should make it the drug of choice. 5% of patients with pneumococcal pneumonia still die, but this is due to host factors rather than lack of bacterial response to the drugs.

Staphylococcal pneumonias are of the greatest importance when they occur with influenza virus infection, though they may occur independently. The combination presents great therapeutic difficulties: (1) the staphylococcus is often resistant to penicillin, (2) the nature of the inflammatory reaction makes the cocci difficult of access by the drug, (3) death may be due to the toxicity of the virus, (4) the rapidity of the onset of the disease. A combination of penicillin and streptomycin is advised until sensitivity results are available. Erythromycin should be added in fulminating cases. Virus pneumonias, except fulminating influenza and psittacosis are usually mild and the value of the tetracycline and chloramphenicol is doubtful.

The aetiology of acute bronchitis and bronchiolitis in infants and young children is discussed and found to be still obscure. No pathogenic bacteria were recovered in 37% of 62 cases in one study quoted [this *Bulletin*, 1958, v. 33, 209]. Unless bacterial investigation shows the need for other drugs penicillin or a drug of the tetracycline group should be used.

In adults the presence of acute bronchitis as a complication of chronic bronchitis and emphysema is, in Great Britain, a very serious problem. The associated organisms show some variation at different times, and in the series reported by different reputable workers, pneumococci, *Haemophilus influenzae* and *Staphylococcus aureus* are the most important, but they are not the primary causes. The author prefers penicillin either alone or with oxytetracycline. Chloramphenicol is preferred by some workers [*ibid.*, 1957, v. 32, 721; 1958, v. 33, 101]. A lack of enthusiasm for prophylactic antibiotics such as oxytetracycline is expressed.

[This is an admirable review of the present treatment of these infections by an acknowledged expert on the subject.]

F. H. Young

Cherniack, N. S., Vosti, K. L., Dowling, H. F., Lepper, M. H. & Jackson, G. G. **Long-Term Treatment of Bronchiectasis and Chronic Bronchitis. A Controlled Study of the Effects of Tetracycline, Penicillin, and an Oleandomycin-Penicillin Mixture.** *Arch. Intern. Med.* 1959, Mar., v. 103, No. 3, 345–53. [16 refs.]

The design of this study as well as the results are similar to those of the Medical Research Council investigation (*Brit. Med. J.*, 1957, v. 2, 255). 67 patients with chronic bronchitis or bronchiectasis, randomly selected by a double-blind technique, were placed in 4 comparable groups and treated orally with tetracycline, a combination of oleandomycin and penicillin, penicillin, and a placebo respectively for 3 to 22 months. The results were assessed on the basis of number and duration of acute lower respiratory illnesses, volume and purulence of sputum, bacteriological findings, gain in weight, improvement in pulmonary function, and decrease in C-reactive protein. Tetracycline emerged as the most effective antibiotic in respect of reduction of acute respiratory attacks and the frequency of isolation of *Streptococcus pneumoniae* and coagulase positive staphylococci, but the frequency of isolation of *Haemophilus influenzae* was not significantly reduced. The patients treated with the oleandomycin-penicillin combination had fewer days of lower respiratory illness than those on penicillin alone. Therapy with penicillin alone was no more effective than placebo therapy. There was no significant reduction in sputum volume or purulence, no significant gain in weight, no improvement in pulmonary function, and

no significant reduction in C-reactive protein, in patients on antibiotic therapy.

A longer period of observation is obviously required before the effects of antibiotics on underlying bronchitis and bronchiectasis can be determined.

H. Stanley Banks

SCHMID, M. Zur histologischen Diagnose und Differentialdiagnose der Virushepatitis und ihrer besonderen Verlaufsformen mit der Nadelbiopsie. **[Histological Diagnosis and Differential Diagnosis of Virus Hepatitis and its Atypical Forms by Needle Biopsy]** *Schweiz. med. Woch.* 1959, Aug. 8, v. 89, No. 32, 830–37, 16 figs. [Numerous refs.]

"The problems of histologic diagnosis and differential diagnosis of virus hepatitis on the basis of histological material obtained by needle biopsies are thoroughly discussed; special attention is given to atypical forms.

"The characteristic polymorphological histological picture is pronounced in most forms. This is true in the majority of cases, even with cholostatic hepatitis which is attributable to a functional disturbance of the intrahepatic bile ducts (hepatitis with a cholostatic tinge after *Kalk*). A few cholostatic hepatitis cases however do not demonstrate the typical liver cell and mesenchymal changes characteristic of virus hepatitis. Morphologically they cannot be distinguished with certainty from the cholostatic hepatosis ('cholangiolitic hepatitis' of *Watson* and *Hoffbauer*).

"While the acute form of virus hepatitis can be easily diagnosed with a 'blind' needle biopsy, chronic hepatitis demands a selective biopsy carried out under laparoscopic control because chronic hepatitis with its profuse scar tissue often demonstrates focal changes."

KUNIN, C. M. **Serum Hepatitis from Whole Blood: Incidence and Relation to Source of Blood.** *Amer. J. Med. Sci.* 1959, Mar., v. 237, No. 3, 293–303. [10 refs.]

This study was undertaken in 2 Veterans Administration hospitals in the Boston area to determine the relation between an apparent increase in incidence of serum hepatitis noted in certain years and the purchase of whole blood from a particular commercial source. The study was undertaken when the occurrence of 7 cases of serum hepatitis at one of the hospitals in a single year caused concern as to the possibility that this source was responsible.

Good records were available and these were employed to determine the relation of various sources of blood to the occurrence of cases of serum hepatitis at one hospital and to make a comparison of the suspected source and all others as causing cases. These results suggested a relation between the use of blood from the suspected bank and the occurrence of serum hepatitis but this alone hardly constituted a case against the bank so that the records of another hospital also receiving blood from the suspected source were similarly investigated. This second hospital used as much blood in 1 year as the first did in 4 years and the investigation revealed that the use of blood from the suspected bank coincided closely in time with the appearance of an increased number of cases of serum hepatitis. Moreover the amount from this bank that was used in cases of serum hepatitis was proportionately greater than that given to all recipients from any other source or from all sources.

In the course of his investigation 2 interesting assumptions were made by the author, (a) that the most valid estimate of the number of icterogenic pints used when multiple transfusions are given is based on the number of cases of serum hepatitis per 100 pints of blood given, regardless of the number of pints received by the individual recipients, and (b) that a single pint was responsible for each case and the remaining pints received were not icterogenic. Inadequate screening of donors or recruitment of the latter from a population with an unusually high incidence of carriers, or both, were regarded as the factors responsible for making blood from the suspected bank unsuitable.

A. Joe

KLIJN, L. C. De serologische diagnostiek van mononucleosis infectiosa. **[The Serological Diagnosis of Infectious Mononucleosis]** *Nederl. Tijdschr. v. Geneesk.* 1959, Aug. 1, v. 103, No. 31, 1575–8. [12 refs.]

The English summary appended to the paper is as follows:—

"The results yielded by the original technique of the Paul-Bunnell test are not sufficiently reliable to establish the diagnosis of infectious mononucleosis beyond doubts; moreover they are not specific for that disease. When performed with serum which has been previously subjected to absorption by guinea pig kidneys, however, the Paul-Bunnell test is highly specific for the serological diagnosis of infectious mononucleosis, and therefore indispensable. A positive result of the test applied in this manner constitutes a serological confirmation of the diagnosis, whatever the titer."

GARDNER, C. C., Jr. **Acute Pericarditis as the Initial Manifestation of Infectious Mononucleosis.** *Amer. J. Med. Sci.* 1959, Mar., v. 237, No. 3, 352–8, 4 figs. [37 refs.]

This is the case history of a male, aged 22 years, who developed symptoms and signs characteristic of acute pericarditis except that pericardial friction was never heard. The diagnosis was supported by electrocardiographic examination. On the 10th day of illness the typical signs of glandular fever supervened, with inflamed throat, generalized lymphadenopathy and a macular erythema on body, head, and extremities. Haematological examination supported the diagnosis of glandular fever and the Paul Bunnell test was strongly positive. From the text it appears that recovery took place about 1 month after the beginning of the pericarditis.

The author presents the case as one of acute pericarditis followed 10 days later by clinical infectious mononucleosis and claims that it is only the fifth

recorded example of pericarditis being the initial manifestation of the disease [this *Bulletin*, 1953, v. 28, 1020; 1957, v. 32, 1134; 1958, v. 33, 642]. He believes that acute pericarditis is one of the varied manifestations of infectious mononucleosis. *A. Joe*

WATSON, K. C. **Acute Purulent Meningitis.** *South African J. Lab. & Clin. Med.* 1959, Mar., v. 5, No. 1, 49–55. [14 refs.]

This is a review of the treatment of 83 patients, 68 Bantu and 15 Indians, seen during 1956–7 in the King Edward VIII Hospital, Durban: all were bacteriologically diagnosed. There were 35 patients with pneumococcal, 17 with *Haemophilus influenzae* and 25 with meningococcal meningitis: of the remaining 6, 1 had coliform, 4 salmonella and 1 proteus meningitis. All were treated initially with penicillin and a sulphonamide: on bacteriological diagnosis the treatment was changed according to the organism. In pneumococcal meningitis a broad-spectrum antibiotic was added to the penicillin and sulphonamide: 23 out of 35 patients died—11 of those who died were under 1 year old, 8 were over 15. *H. influenzae* meningitis was treated with chloramphenicol and streptomycin: 16 out of 17 patients were under 1 year old, and 11 died. Meningococcal infections were treated with penicillin and sulphonamides and 2 out of 25 patients died: no patient was under 6 months old and only 2 under 1 year. Of the 6 patients with coliform, proteus or salmonella infections 5 died.

The author is inclined to be against the use of intrathecal penicillin in any type of infection though some of his patients had one dose of penicillin intrathecally. He is reasonably satisfied with his mortality figures except for *H. influenzae* meningitis: he feels that the late stage at which these children are admitted is the main cause of the high mortality.

A. B. Christie

PLATOU, R. V., RINKER, A. & DERRICK, J. **Acute Subdural Effusions and Late Sequelae of Meningitis.** *Pediatrics.* Springfield, Ill. 1959, May, v. 23, No. 5, 962–71, 4 figs. [15 refs.]

Although occasional cases of subdural haemorrhage complicating acute pyogenic meningitis have been reported in the past 20 years (*e.g.* BANKS and MCCARTNEY, *Lancet*, 1942, v. 1, 219), it is only since 1950 that subdural collections of fluid have been recognized as a regular complication of bacterial meningitis in infancy [MCKAY *et al.*, this *Bulletin*, 1950, v. 25, 986]. This article is a major contribution to the subject since it reports as many as 55 cases diagnosed among 343 consecutive patients under 3 years of age admitted to hospital in Louisiana with acute pyogenic meningitis. Such a high proportion could never have been diagnosed, had not the doctors treating the cases been acutely aware of the condition, and of the features which indicate a diagnostic subdural puncture through the lateral angles of the fontanelle, or the coronal sutures. These diagnostic features include convulsions, focal neurological signs, persistent fever or bulging fontanelle or other sign of unsatisfactory clearing up, rapidly increasing head size, projectile vomiting, and opisthotonus—any of these particularly in young infants admitted late in the acute stage of meningitis. Of the 55 cases with subdural effusion, 24 occurred among 113 cases of *Haemophilus influenzae* meningitis, 7 among 28 with pneumococcal meningitis, 1 among 12 with meningococcal meningitis, 8 among 20 with other forms of acute bacterial (non-tuberculous) meningitis, and 15 among 119 cases in which no causal organism was found, probably, in most of them, because of early chemotherapeutic treatment before admission.

In this series it was clearly shown that the presence of early subdural effusions is related to the frequency and severity of neurological sequelae. The subdural fluid probably reflects the occurrence of various localized or diffuse neurological or vascular lesions of the central nervous system, which are responsible for such sequelae as behaviour problems, emotional instability, functional localized nervous defects, retarded development, convulsions, and hydrocephalus. In the majority the subdural effusion cleared up satisfactorily, but it is worthy of note that among 10 patients in whom the same organism was found in the spinal fluid or peripheral blood *and* in the subdural fluid, only 3 escaped with no sequelae and 3 had severe and 4 mild sequelae.

H. Stanley Banks

THRUPP, L. D., FORESTER, Helen E. & BRODY, J. A. **Poliomyelitis in the United States, 1957.** *Pub. Health Rep.* Wash. 1959, June, v. 74, No. 6, 535–45, 5 figs. [12 refs.]

The incidence of paralytic poliomyelitis during 1957 in the United States was 1·5 per 100,000 and was the lowest since 1942. There were no large local outbreaks and the attack rates were low in every region of the country. 5,485 cases were reported, 2,499 paralytic, 2,826 non-paralytic and 160 unspecified. Almost one-half of the paralytic cases were in children under 5 years of age. The peak of the paralytic cases was reached at the end of September while the non-paralytic cases reached a peak in early August. At ages under 20 years the incidence of paralytic poliomyelitis was greater among males than females, 1,011 and 731 cases respectively, at ages 20–40 the position was reversed and 230 females and 211 males were attacked, at ages over 40 there were 42 males and 26 females attacked. The paralytic attack rate [? per 100,000] among the non-vaccinated children under age 5 was 92·8 and 9·6 for children who had received 3 doses of vaccine, at ages 5–9 the attack rates were 56·5 for the non-vaccinated and 9·2 for the triply vaccinated children and for all ages under 40 years the rates were 28·2 and 7·1. The percentage of the total cases which were paralytic was 56 for the non-vaccinated and 25 for the persons who had completed the 3 vaccinations. 3 deaths were recorded in a triply vaccinated group.

The authors doubt whether the widespread use of vaccine was alone responsible for the low incidence in 1957. They suggest that further efforts to complete the 3-dose programme is necessary in large sections of the population at present incompletely vaccinated, particularly the under-fives and the non-white population.

W. J. Martin

KUBRYK, D. **Paralytic Poliomyelitis Trends, 1957.** *Canadian J. Pub. Health.* 1959, June, v. 50, No. 6, 223–7, 1 fig.

The trends in the incidence of paralytic poliomyelitis in Canada as revealed in official statistics up to the year 1957 are presented. Up to 1957 there had been a steady fall in incidence from the peak year of 1953 but the case fatality rate did not show a similar fall. The fall in incidence since 1954 has been most marked in children aged 5–19 and less marked in adults and pre-school children. This change may be related to the greater use of poliovaccine among schoolchildren, it being estimated that 80% of people aged 5–19 were vaccinated against 60% of younger children and 8% of adults. In 1957 there were 96 cases of paralytic poliomyelitis in children aged 0–9, only 6 of whom had had 3 or more doses of poliovaccine, although 24 had had at least 1 dose. There were 7 cases with an onset within 30 days of vaccination and 2 of these were paralysed in the vaccinated limb. Although the case fatality rate was slightly higher in 1956 than in 1954 there was a decline in the percentage distribution of deaths for schoolchildren but a substantial increase for adults.

[In an editorial in the same issue of the journal figures for 1958 are given. There were more cases in 1958 owing mainly to 2 outbreaks, 1 in Manitoba and 1 in Quebec, which between them accounted for 73% of the cases. The incidence continued to decline in the 5–19 age-group but increased in the pre-school children. 44 of the total of 253 cases occurred in children aged 5–9 and no less than 31 of these were in children aged 5 and 6. The case fatality rate in the pre-school children was low, 4·5 against 23·5 in adults aged 20–39. 19 of the 253 patients had received 3 doses of poliovaccine. It was concluded that the vaccine is effective but that greater efforts are required to vaccinate pre-school age children and adults. To this end combined polio, diphtheria, tetanus and whooping cough vaccination of infants is recommended.]

A. J. Beale

BERNI, A. Nota sulla poliomielite a Roma nel 1958. [**Poliomyelitis in Rome in 1958**] *Nuovi Ann. d'Igiene e Microbiol.* 1959, Jan.–Feb., v. 10, No. 1, 37–45. [27 refs.] English summary (4 lines).

Tables are given of population, notifications and case mortality rates for poliomyelitis in Rome from 1935 to 1958 (in the latter for 11 months only) and the monthly incidence for the decennium 1948–57 is compared with that for 1958. From 1935 to 1950 the case mortality rate showed in general a falling tendency, then between 1951 and 1957 remained relatively stationary (with fluctuations) around 4%, but in 1958 the rate rose very sharply to 17·24%.

Between 1948 and 1957 the annual number of cases increased gradually until the year 1956, when the number was 174, in 1957 it was 215, but in 1958 it was 458. The monthly incidence also showed a change as in the decennium 1948–57 the greatest incidence was in July with a lesser peak in October–November, but in 1958 the greatest incidence was in October, the rises between June and October being very sharp.

The case mortality for the 39 cases in June and July was over 40%, it then fell gradually but had a final rise in November to 17·5%.

All the cases were of the paralytic type, the fatal ones being bulbo-spinal; the age-group 0–6 was attacked in 90% of cases though both in 1957 and 1958 those over 13 years formed 5·6%. The virus was type 1. Investigation of urban, suburban and rural areas of the city showed patchy distribution, and there appeared to be no correlating epidemiological factors. In view of this, details are being collected for the same period from the whole province.

In view of the high incidence in the 0–6 age-group the author suggests that vaccination in the second half of the 1st year may be advisable.

[This is an extremely high case mortality rate and in view of the increasing incidence in the previous 2 years, information on the type of virus found in 1956 and 1957 would be of interest.

According to a note on pp. 254–55 of *Igiene e San Pubblica*, 1959, v. 15, 1958 was an epidemic year throughout Italy.] *W. K. Dunscombe*

WISNER, B., MARCOVICI, M., BUIMOVICI, Elena, with the collaboration of I. ALEXA & A. POPESCO. Étude épidémiologique et virologique d'une épidémie de poliomyélite dans une crèche. [**An Epidemiologic and Virologic Study of a Poliomyelitis Epidemic in a Creche**] *Arch. Roumaines Path Expér. et Microbiol.* 1958, Sept.–Dec., v. 17, Nos. 3/4, 471–82, 1 fig. [26 refs.]

An outbreak of poliomyelitis in a day nursery in Bucharest is described. The nursery was for 20 children up to 3 years housed in 2 rooms. In the same building were 2 other groups of children staying for long periods. The outbreak was confined to the day nursery, and 9 of the 20 children became clinically infected. The outbreak was due to Type 1 poliovirus which was isolated from 7 of the 9 patients and 4 of 8 contacts examined. No viruses were isolated in HeLa cells or suckling mice from the adult staff or from the children in the other 2 sections of the building. 5 days before the onset of the first case, French killed poliomyelitis vaccine (Institut Pasteur) was administered to the children. 2 out of 6 vaccinated and 7 out of 14 unvaccinated children were paralysed. The outbreak was not ascribed to the vaccine because it was also given to the other children in the institution and to several thousand children in Bucharest without accident. *A. J. Beale*

SEMASHKO, A. M. **The Spread of Poliomyelitis in Latvia.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 9/10, 1497–1500, 3 figs. [Translated from Russian.]

This paper contains an account of the epidemiology of poliomyelitis in Latvia. Periods of increased incidence appeared to last for 2–3 years and there has been a steadily upward tendency for the number of cases in inter-epidemic years. Epidemics occur in the late summer as is found with enteric diseases. The disease has been more prevalent in the northern part

of Latvia than in the southern part. One of the most striking features of poliomyelitis in Latvia is the high incidence of the disease in schoolchildren and adults, in 1955, for example, half the cases were in children under 7 years [the table showing the percentages at various ages contains errors of addition]. In rural areas there was a tendency for there to be a lower incidence in pre-school children and a higher incidence in schoolchildren than was found in the larger towns. [It is noted that the predominant clinical forms of poliomyelitis are abortive and atypical. The figures presented in the paper would be more valuable if they were divided into paralytic and non-paralytic cases.]

A. J. Beale

Paktoris, E. A. & Vorontsova, L. A. **Incidence of Poliomyelitis in Lithuania, 1955: Clinical and Epidemiological Characteristics—I.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1957, v. 28, Nos. 9/10, 1500–505, 2 figs. [Translated from Russian.]

In this account of the incidence of poliomyelitis in Lithuania in 1955 attention is drawn to the importance of nurseries and nursery schools in the spread of poliomyelitis. It was found that the incidence of paralytic poliomyelitis was 2·4 times as high in children at day nurseries as in children not attending these nurseries up to the age of 3 years. The incidence was 9 times higher for children attending nursery schools in the age group 4–7 compared with children not attending these schools. *A. J. Beale*

Levy, D. & Falk, W. **Poliomyelitis under One Year of Age. Clinical and Laboratory Findings in a Group of 529 Patients with Poliomyelitis younger than One Year of Age.** *J. Dis. Children.* Chicago. 1959, June, v. 97, No. 6, 829–38.

Between the end of 1949 and the end of 1956, 529 infants under 1 year old were admitted suffering from poliomyelitis to the Rambam Government Hospital, Haifa. The total for all ages was 1,527 and infants under 1 year old represented between 27 and 43% of yearly admissions. All clinical types were represented and 71 babies died. Of the 529, only 25 babies were under 3 months old. The cellular and protein content of the cerebrospinal fluid was studied in some detail. The findings did not support the view that cells are high and protein low in the early stages and the reverse in the later stages. Severity of clinical findings was not related to any changes in the cerebrospinal fluid. Signs of meningeal irritation were not related to changes in the cerebrospinal fluid: some infants with abnormal fluids had no meningeal signs, others with marked meningeal signs had normal fluids.

A. B. Christie

Depoux, R. & Orio, J. Note sur une petite épidémie de poliomyélite à Port-Gentil (Gabon). [**A Small Epidemic of Poliomyelitis in Port-Gentil, Gabon**] *Bull. Soc. Path. Exot.* 1958, July–Aug., v. 51, No. 4, 601–7.

After the appearance of 8 cases of poliomyelitis (all but 1 in infants between 1–2 years), a small serological survey was carried out in the area of Port Gentil in Gabon.

Only type 1 poliovirus has been isolated in the area but the survey of 175 sera revealed that antibodies to all 3 types were rapidly acquired. At 11–15 years all 16 children had type 1 antibodies and all but one those to type 2 and 3. Even between 2 and 5 years the majority of children had antibodies to individual types —thus the incidence was type 1, 93%, type 2, 78% type 3, 56%.

The authors note that the standards of hygiene were extremely primitive and that diseases spread by water and arthropods were very prevalent. *A. J. Beale*

Walley, R. V. **Assessment of Respiratory Failure in Poliomyelitis.** *Brit. Med. J.* 1959, July 25, 82–5, 1 fig. [20 refs.]

Thomson, W. O. & Fletcher, D. J. B. **Immediate Sensitivity Reaction to Poliomyelitis Vaccine.** *Brit. Med. J.* 1959, July, 11, 39–41, 1 fig.

A nurse with a history of sensitivity to penicillin and to a lesser extent streptomycin developed a severe reaction to 1 ml. of poliovaccine (Parke, Davis). Within 5 minutes generalized itchiness and watering eyes developed. She also had severe colicky pains in the abdomen and a desire to micturate. She was on the point of collapse. Her eyes were almost closed by oedema, but there was a rapid response to adrenaline. About 6 weeks later she received 0·1 ml. of poliovaccine (Pitman-Moore) intradermally and again developed an immediate sensitivity reaction. Her eyes were again oedematous and she was nauseated, trembling and had buzzing in the ears. She again responded to adrenaline.

The manufacturers of the vaccines are named, but it is noted that vaccine from all manufacturers employing penicillin in the culture media will contain penicillin in variable amounts. *A. J. Beale*

Tobin, J. O'H., Brunner, K. T. & Syverton, J. T. **Studies on the Propagation *in vitro* of Polioviruses. IX. Application of HeLa Cell Cultures to study of the Distribution of Poliovirus Antibody naturally present in a Population or induced by Administration of Formalinized Vaccines.** *Amer. J. Hyg.* 1959, May, v. 69, No. 3, 214–23, 2 figs. [12 refs.]

The response of 329 subjects to killed poliovaccine administered in 1955–6 is reported. The results confirm those of Salk [*Ann. New. York Acad. Sci.*, 1955, v. 61, 1023; this *Bulletin*, 1955, v. 30, 573] and later investigators. The response to the vaccine (several batches of commercially available vaccine were equally good) was good, 93% of individuals without antibodies responding. Almost all of 65 triple negative subjects responded to all 3 types (3 type 1, 1 type 2 and 3 type 3 failures occurred).

Heterologous antibodies enhanced the response except

that types 1 and 3 antibodies had little cross enhancing effect. The presence of homologous antibodies either natural or vaccine-induced led to a booster response. The response was better to 2 doses at intervals of 4 weeks than to 2 doses at intervals of 3 weeks or 3 doses at monthly intervals. Antibody levels declined after 1 year, the geometric mean titres in a group of 31 triple negatives were type 1, $^1/_{33}$, type 2, $^1/_{84}$ and type 3, $^1/_{47}$ 2 weeks after primary vaccination and $^1/_4$, $^1/_{11}$ and $^1/_4$ respectively 1 year later. The response to a third dose several months after the primary course boosted antibody titres to levels similar to those found after clinical poliovirus infection. *A. J. Beale*

MELÉN, B., WESSLÉN, T. & OLIN, G. **Results of an Experimental Vaccination against Poliomyelitis.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 1, 11–24, 1 fig. [13 refs.]

This paper records the results obtained with the first poliovaccine made in Sweden in which human embryonic tissue cultures were used to grow the virus. The potency was less than that obtained at present and the method of manufacture now employed is very different. Studies with these early batches either as a trivalent or a monovalent vaccine demonstrated the importance of pre-immunization antibodies and spacing of the injections on the response to poliovaccine. The response was much better in children with antibodies than in triple negative children. Not only did prior antibodies to any type enhance the response to that type but also type 2 antibodies improved the response to type 1 or 3 and *vice versa*. The intradermal route of vaccination was not as satisfactory as the subcutaneous. The response of children given a second dose after 6 weeks was superior to that of children given their second dose of vaccine after 3 weeks. Monovalent vaccines had very similar effects on antibodies to the homotype as trivalent vaccine. They had little or no effect on antibodies of other types.

In triple negative children dilution of vaccine produced a proportionally lesser effect, but dilutions of vaccine in children who had heterotypic antibodies were more effective than would be anticipated from the results in triple negative children. *A. J. Beale*

WOLF, A. M., SHAUGHNESSY, H. J., JANOTA, Martha, CHAPMAN, J. W., CHURCH, Ruth E. & MOORE, Mildred. **Duration of Seroimmunity after Injection with Ultraviolet-Irradiated Poliomyelitis Vaccine. Role of Booster Inoculations.** *J. Amer. Med. Ass.* 1959, June 6, v. 170, No. 6, 650–52.

The first batches of vaccine were made by the authors by inactivation with ultraviolet light and heat] this *Bulletin*, 1956, v. 31, 1198; *ibid.*, 1958, v. 33, 892] but subsequently a commercial vaccine prepared with formalin and ultraviolet light was also used. This commercial vaccine was of greater potency. Before vaccination 92, 80 and 84% of the children lacked antibodies to types 1, 2 and 3 poliovirus. After the primary course these figures were reduced to 12, 0 and 17% respectively with mean titres of 1 in 48, 1 in 82 and 1 in 72 to types 1, 2 and 3 respectively. 1–3 years later these mean titres had fallen to 1 in 12, 1 in 73 and 1 in 42. Many children lacked antibodies to types 1 and 3. However, after a booster dose the mean titres were raised to 1 in 182, 1 in 328 and 1 in 147. 2 years later these levels had again declined to 1 in 13, 1 in 50 and 1 in 17 respectively and 9% lacked type 1 and 14% type 3 antibodies. Another booster dose again raised the titres to still higher levels.

It is concluded that the ultraviolet inactivated vaccine is immunogenic, that booster injections are desirable, and that the serological immunity is probably quite durable. *A. J. Beale*

HORSTMANN, Dorothy M., NIEDERMAN, J. C. & PAUL, J. R. **Attenuated Type 1 Poliovirus Vaccine. Its Capacity to Infect and to Spread from "Vaccinees" within an Institutional Population.** *J. Amer. Med. Ass.* 1959, May 2, v. 170, No. 1, 1–8, 6 figs. [19 refs.]

In this paper Dr. Horstmann and her colleagues describe careful investigations into the performance of attenuated poliovirus in man. 3 trials were carried out in an institution caring for adults and children. The test population varied in age from 4 to 24 years and was divided into 2 separate units. Before the commencement of the trial all the subjects were either naturally immune or had received 2 doses of killed vaccine in the previous 6 months. Sabin's L-Sc type 1 poliovirus was used by mouth for all the trials. This virus pool had been purified by terminal dilution, since then Sabin has reported selection of attenuated variants from this population by means of plaque isolation [this *Bulletin*, 1957, v. 32, 1032]. The 3 trials were designed to answer 5 questions.

(1) Whether children with some degree of immunity can be infected with attenuated poliovirus. It was found by using a dose of 25 million TCD50 that infection was readily induced in children as judged by faecal excretion, but that if the infecting dose was contained in a capsule then pharyngeal infection was prevented.

(2) The difference in response to virus administration of children whose antibodies had been acquired naturally or as a result of killed poliovaccine. In the first trial it was found that 10 out of 10 children who had received killed poliovaccine were infected with the attenuated strain of poliovirus. This led to excretion in the pharynx as a rule if the virus was given in milk and in the faeces in high titre. It was accompanied by a complement-fixing antibody response and by a rise in the neutralizing antibody titre. The vaccine-immune children had antibody levels varying from less than 1/4 (in 3 children) to 1 in 64 (as measured by the colorimetric method). By contrast only 2 out of 9 naturally immune children became infected and in them virus excretion was limited to the faeces and was of much shorter duration. These children before virus administration had antibody levels in the range 1/32 to 1/1024 (the pre-feeding titre of the 2 children who became infected was 1/32 and 1/64).

(3) The effect of dosage upon infection with attenuated polioviruses. 16 weeks after the first trial attempts were made to re-infect 11 of the children, 6 of whom were originally immune from vaccination and 5 from natural infection. The same large dose (25 million TCD50) of virus was administered. All 11 became re-infected as judged by the excretion of poliovirus on one or more occasions in the faeces. However, excretion was of a much lower level and only 2 excreted virus in the throat and both of these were vaccine-immune children who had received their first dose of attenuated virus in a capsule. As a result of this trial and of the previous one showing a difference in resistance of the alimentary tract in naturally immune and vaccine-immune individuals the authors believe that such resistance of the pharynx or the lower alimentary tract may be mediated by local immunity rather than circulating antibody.

In the third trial 16 individuals were divided into 4 groups given falling dilutions of virus. The first group received 25 million, the next 250,000, the next 2,500 and the last 250 TCD. 7 out of 8 of those given the 2 larger doses excreted virus in the stools, 4 of them for long periods, and these same 4 showed an antibody rise. 3 of the 8 given the lower 2 doses had virus in the stools for short periods.

(4) The degree of spread of virus to contacts. In the first trial there were 49 contacts and only 1 out of 36 naturally immune contacts became infected whereas 12 out of 13 of the vaccinated contacts did become infected. None of the children administered attenuated virus, nor any of the naturally infected contacts, were ill. Virus appeared in the faeces, 1–3 days after administration, and appeared in contacts in some instances within 7 days after administration to the first children.

(5) The neuropathogenicity of the virus fed and the virus excreted was tested by intracerebral inoculation into monkeys. The last positive stool specimen from 25 subjects was tested by using virus that had been given 2 passes in monkey kidney tissue culture at a low level of bicarbonate. These conditions were deliberately chosen to select any virulent mutants that might have appeared. Whereas 1 of 14 monkeys infected with the fed virus developed paralysis, 5 out of 67 monkeys inoculated with the excreted virus became paralysed. In addition there were 5 monkeys that showed lesions in their CNS but did not become paralysed. The authors believe that their results will be useful in interpreting the results of larger field trials on open communities. They believe that such field trials should be undertaken.

[The detailed results of the antibody responses are not given. The relative role of circulating antibody and local immunity in determining whether re-infection will take place with polioviruses requires further investigation. It was concluded from these trials that local immunity conditioned whether intestinal or pharyngeal infection with polioviruses occurred. However, the 2 children who were naturally immune but re-infected in the first trial had antibody levels of 32 and 64 which are at the low end of the range for naturally immune children and the high end for killed vaccine. The case would not therefore seem to be proved.] *A. J. Beale*

PLOTKIN, S. A., JERVIS, G., NORTON, T., STOKES, J., Jr. & KOPROWSKI, H. **Persistence of Antibodies after Vaccination with Living Attenuated Poliovirus.** *J. Amer. Med. Ass.* 1959, May 2, v. 170, No. 1, 8–12. [19 refs.]

This paper deals with the persistence of antibodies after vaccination with attenuated poliovirus by mouth some years earlier. 3 groups of children are discussed.

(A) 7 children vaccinated with the rodent-adapted TN type 2 virus in 1950 and 1951. All these children had antibodies 8 years after vaccination, ranging from 1/16 to 1/128 against type 2 poliovirus.

(B) These 7 children were vaccinated with the SM N-90 strain of type 1 poliovirus adapted to chick embryos. 4½ years after vaccination they all had antibody levels ranging in titre from 1/16 to 1/512. These levels were very little different from those found 1–3 months after vaccination.

(C) The SM strain of type 1 was given to 7 infants, all of whom have maintained high levels of antibody 15 to 28 months after administration. 1 of these children was also given the TN type 2 strain and this infant also retained antibodies to type 2 virus. In addition TN strain was given to 2 other children, who also retained high levels of antibodies about 2 years after virus feeding. Similarly 2 infants were given the CHAT type 1 strain and again all these retained antibodies for at least 1 year. 2 infants received the Fox strain of type 3 virus and 1 of these had antibodies 14 months later whereas the other had no demonstrable type 3 antibodies. This infant was re-fed with the Fox strain of poliovirus and developed an antibody titre of 1/64. Although virus was isolated from the faeces of this infant it was in much lower titre than following the first virus feeding.

The infants in this trial varied in age from 5 days to 6 months but neither the immunological immaturity nor the maternal antibody appeared to interfere with the response to attenuated poliovirus. The response to the poliovirus had, however, to be assessed in the presence of high levels of transplacental antibody by the failure to observe the expected rate of fall-off in antibody titre. The possibility was considered that booster infections by naturally occurring poliovirus infection contributed to the persistence of antibodies. It was found that a third of the children in groups A and B and 24% of the children in group C had evidence of infection with types of poliovirus other than those fed. The authors conclude that their evidence lends support to the theory that antibody levels will persist indefinitely in most subjects infected with living poliovirus. They also believe that the local immunity of the intestinal tract will probably persist longer than the antibodies in the blood. *A. J. Beale*

BARR, R. N., BAUER, H., KLEINMAN, H., JOHNSON, E. A., MARTINS DA SILVA, M., KIMBALL, Anne C. & COONEY, Marion K. **Use of orally administered Live Attenuated Polioviruses as a Vaccine in a Community Setting. A Controlled Study.** *J. Amer. Med. Ass.* 1959, June 20, v. 170, No. 8, 893–905, 4 figs. [13 refs.]

This valuable paper reports a carefully controlled study of the use of attenuated poliomyelitis vaccine developed by Lederle Laboratories. The study was carried out among married students studying at the University of Minnesota and their families. In all, 551 individuals were studied. Roughly one-half of these had had 3 doses of Salk-type poliovaccine before the beginning of the study. The biggest deficiencies in poliovaccination were among the very young children and the fathers.

The families in the study were divided into groups and in the first phase the first group were given a placebo substance while the second group received feedings of attenuated polioviruses in gelatin-coated capsules in the order type 2 (10^5 TCD50), type 1 (7×10^4 TCD50) and finally type 3 (2×10^5 TCD50). The feedings took about 76 days and then the procedure was reversed—the first group getting feedings of virus and the second group the placebo. It was found that the incidence of illness in the 2 groups was the same, there being no evidence of any illness attributable to the vaccine. The trial was carefully conceived so as to avoid bias in the clinical or laboratory staff.

The response to poliovaccine feeding in children was very good: 89·7% for Type 1, 87·5% for Type 2 and 85·5% for Type 3 of the people without prior antibodies showed some response. These figures were lower, around 70%, when confined to those showing a 16-fold or greater (2 tubes or more) antibody response. The response of individuals who were triple negative is not recorded. The response of adults and of children and of infants with passively acquired antibodies was considerably less—for example, only 15% of the adults responded to Type 1 virus with a 16-fold or greater rise in antibody level and the response was worse in individuals with prior antibodies. Although the evidence is not presented in detail it is stated that prior Salk-vaccination did not prevent alimentary infection with attenuated polioviruses whereas naturally acquired antibodies did. It was also stated that children who had been vaccinated with Salk-vaccine but showed no serological response (this was 57% for Type 1 virus) showed a good response to the attenuated strains of poliovirus. Virus was excreted by people responding to the vaccine and occasional examples of inter-family spread of virus were noted. Intra-family spread of virus was not noted since the whole family was vaccinated at the same time.

[This study shows that the vaccine comprising strains of attenuated poliovirus is safe and effective in producing antibodies. Its effectiveness in the best responding group of children is no better than that achieved with the best preparations of Salk-type vaccine [this *Bulletin*, 1958, v. 33, 288]. However, much of the Salk-vaccine at present available is of suboptimal potency as revealed by the figures of individuals lacking antibodies after a full 3-dose course of vaccine in this study, which were 57% for Type 1, 20% for Type 2 and 77% for Type 3. This paper also illustrates a difference between the response of people with previous antibodies to Salk-type vaccine and to attenuated vaccine. The presence of prior naturally acquired antibodies leads to a booster response to a Salk-type vaccine whereas it inhibits the growth and antibody response to attenuated vaccine.] *A. J. Beale*

Abad-Gómez, H., Piedrahita, F., Solórzano, R. & Martins Da Silva, M. **Communitywide Vaccination Program with Attenuated Poliovirus in Andes, Colombia.** *J. Amer. Med. Ass.* 1959, June 20, v. 170, No. 8, 906–13, 4 figs. [18 refs.]

In the early part of 1958 there was a small outbreak of poliomyelitis in southern Antioquia in Colombia. When the public health officials appealed to the Pan American Sanitary Bureau for help it was decided to use an attenuated poliovaccine because of previous failures of formalinized vaccine in the face of an epidemic. Attenuated poliovaccine prepared by Lederle was therefore fed to about 7,000 individuals under 7 years of age, at a time when 15 cases of poliomyelitis had been reported. There were no untoward effects as a result of giving the vaccine and after the campaign started only 4 additional cases of poliomyelitis were reported in the area and none of these individuals had been given attenuated polioviruses. Antibodies to poliomyelitis virus are acquired at an early age in Colombia and by the age of 7 years over 80% of the children have antibodies to all 3 types of poliovirus. In the vaccinated age-group under 7 years about 13% lacked antibodies to all 3 types of poliovirus. It was found that the response to all 3 types of virus was good (about 80%) in children without detectable antibodies before vaccination. However, the response of individuals with prior antibodies was less good, thus for Type 1 75% with levels between $^1/_4$ and $^1/_{16}$ responded and 43% with levels $^1/_{32}$–$^1/_{512}$.

Although it was impossible to say what effect the vaccine had upon the outbreak of poliomyelitis this trial again shows that attenuated poliovaccine is safe and effective in immunizing children. The authors also stress its advantages for a developing country in that it is relatively cheap to prepare and simple to administer. *A. J. Beale*

Plotkin, S. A., Koprowski, H. & Stokes, J., Jr. **Clinical Trials in Infants of Orally Administered Attenuated Poliomyelitis Viruses.** *Pediatrics.* Springfield Ill. 1959, June, v. 23, No. 6, 1041–62, 2 figs. [38 refs.]

Attempts were made to immunize 46 infants under 6 months of age against poliomyelitis by using attenuated strains of all three types of virus. This paper is very valuable because the details of each child's response to the various attenuated strains fed is presented in detail. One of the strains of poliovirus, the Jackson strain of type 2 adapted to the chick embryo, proved to be non-antigenic for man. All the other strains appeared to be very effective. The response to vaccination was judged by the excretion of virus and by the antibody response. Since the children were under 6 months most of them had passively acquired antibodies so that the antibody response was calculated after allowing for a decline in passively acquired antibodies with a half life of 21 days.

Judged in this way 27 out of 32 infants responded

to feeding with the CHAT strain of type 1 virus at the first attempt and 8 out of 9 with the Wistar strain of type 1. Similarly, 19 out of 22 infants responded to the P-712 strain of type 2 and 26 out of 31 infants who had been fed with the Fox type 3 strain. Subsequent re-feeding was usually successful in establishing an immune response when the first attempt failed.

The most important factor in limiting the response was not thought to be the level of transplacental antibodies but the degree of immaturity of the children. For example, with the CHAT type 1 strain 22 out of 28 feedings were successful in children under 60 days whereas all the feedings (9 out of 9) were successful in children over 60 days. Interference was noted when all 3 types of virus were fed together, usually the Fox strain of type 3 interfering with the establishment of immunity to the other 2 types. However, when the 3 types of poliovirus were fed in sequence with a 3-week interval between them no interference occurred.

The dose of virus that is effective varies from strain to strain, the Fox strain of type 3 appeared to be effective when only 30 TCD were employed whereas for the CHAT type 1 strain 100,000 TCD appeared to be necessary. 3 infants that had responded satisfactorily to a first dose of virus were subsequently re-fed with the same type. 2 of these infants failed to excrete virus at the second feeding and the other child only excreted virus for a short period.

No child showed any untoward reaction to the successive doses of attenuated poliovirus and it is concluded that vaccination of infants under 6 months of age with attenuated strains of poliomyelitis is an entirely safe procedure which is likely to be effective.

A. J. Beale

VERLINDE, J. D., WILTERDINK, J. B. & KRET, A. **Active Immunization against Poliomyelitis with Live Attenuated Viruses.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 8, No. 5, 549–64, 1 fig. [25 refs.]

This paper records another careful trial of Sabin's attenuated strains of poliovirus for immunizing man. 178 persons were vaccinated (the results for the first 40 have been reported separately earlier, VERLINDE *et al.* this *Bulletin,* 1958, v. 33, 1022). The strains were given in the order type 1, 3 and 2, with an interval of 3 weeks between feedings.

Safety. The vaccination proved safe, only 2 reactions occurred, both of an allergic nature. One subject developed paralysis 3 months after feeding, but this was shown serologically to be due to European tick-borne encephalitis.

Alimentary Infection. This was almost universal in triple negative children (1 out of 10 failed to excrete type 1, and 2 failed with type 2) lasting from 1 to 7 weeks. Excretion of virus in those lacking antibodies to the type fed but possessing antibodies to other types was usual, 22 out 33 such opportunities for infection being successful. Excretion of virus was less prolonged and of lower titre in subjects with antibody. Although the presence of antibody clearly reduced the chance of alimentary infection from about 80% for all 3 types to about 35%, this could not be shown to be related to antibody titre. Adults showed a much lower likelihood of infection (10% for those without antibody) regardless of antibody level and age was thought to be an important factor in determining whether infection would take place.

Spread of Infection. This was obviated by vaccinating all members of the family together.

Reversion to virulence of excreted virus. Some slight increase in virulence was noted for the type 3 strain. The alimentary canal does not favour virulent virus since attenuated type 3 strains were sometimes isolated after a relatively virulent isolate.

Immune Response. This was excellent, between 90 and 100% of children made an immune response if they lacked prior antibodies. A few children responded immunologically without virus being detected in the faeces. The response was still good (50–80%) in children with antibodies. In adults despite the fact that only 10% had an alimentary infection, 50% had an antibody response. The level of response of individuals with antibody was on the whole superior to that of those without antibody. It is thought that in nature poliovirus antibody levels are probably maintained by repeated alimentary infections which become less frequent with increasing age because of the development of resistance to alimentary infection not mediated by circulating antibody. It is therefore assumed that immunity resulting from attenuated poliovirus will not be life-long but may have to be boosted by repeated feedings of virus. The response to type 1 was consistently better than that to types 3 and 2. This was ascribed to interference from the type 1 virus fed first. An interval of 4 weeks between feedings is suggested to overcome this.

A. J. Beale

RYDER, D. E., DOANE, Frances W., ZBITNEW, Audrey & RHODES, A. J. **Report of an Outbreak of Bornholm Disease, with Isolation of Coxsackie B5 Virus: Toronto, 1958.** *Canadian J. Pub. Health.* 1959, July, v. 50, No. 7, 265–9. [22 refs.]

An outbreak of Bornholm disease in a Toronto suburb in 1958 is described. 27 patients were studied and 21 yielded a Coxsackie B virus, and all but 1 were typed as Coxsackie B5. The exception was Coxsackie B4. 8 out of 10 patients studied either showed a rise in antibody titre to the type of virus isolated from the stools or a high convalescent titre. 2 patients, despite excreting virus and suffering from symptoms, failed to show an antibody response. Clinically the disease was characterized by an acute onset with fever, pain in the abdomen and gastro-intestinal upset. Neck stiffness was noted in 3 patients. Attention is drawn to the fact that Coxsackie B5 was implicated as the cause of other cases of pleurodynia, abacterial meningitis and pericarditis in Southern Ontario in 1958 (MCLEAN *et al., Canadian Med. Ass. J.*, 1958, v. 79, 789).

A. J. Beale

BELL, J. F. & MEIS, A. **Pericarditis in Infection due to Coxsackie Virus Group B, Type 3.** *New England J. of Med.* 1959, July 16, v. 261, No. 3, 126–8, 2 figs.

SLONIM, D. & HLOUCAL, L. Bildung und Überdauern der komplementbindenden und virusneutralisierenden Antikörper bei der Zeckenenzephalitis. [**Production and Persistence of Complement-Fixing and Neutralizing Antibodies in Tick-Borne Encephalitis**] *Zent. f. Bakt. I. Abt. Orig.* 1959, v. 175, Nos. 5/6, 344–55, 6 figs. [13 refs.]

An investigation has been made in Czechoslovakia of the persistence of antibodies in the sera of 71 persons suffering from tick-borne encephalitis. Complement-fixing antibody usually appeared rapidly, reaching a maximum titre of 64 or 128 after 4–10 weeks and disappearing after 1 year. A titre of 4 was regarded as diagnostic. In some cases the appearance of antibody was delayed until the 3rd or 4th week of illness, and in rare instances the titre remained low, not exceeding 4 throughout the period of observation. Neutralizing antibody appeared at the same rate as complement-fixing antibody, the neutralization index attaining a maximum of 2–4 log units, and a high titre could still be observed 1 year after the onset of illness.

D. J. Bauer

SMITHBURN, K. C., KOKERNOT, R. H., HEYMAN, C. S., WEINBREN, M. P. & ZENTKOWSKY, D. **Neutralizing Antibodies for Certain Viruses in the Sera of Human Beings residing in Northern Natal.** *South African Med. J.* 1959, July 4, v. 33, No. 27, 555–61, 1 fig. [23 refs.]

Sera were collected from children (0–14 years) and adults in a number of mountain, riverine and coastal localities in northern Natal. They were tested in neutralization tests in mice against 13 arboviruses isolated in Africa, many of them in Tongaland. Protection against not less than 50 LD50 virus was regarded as positive. The virus dosages used varied from 3,162 to 3 LD50, but protective sera in tests with less than 50 LD50 were re-tested.

Only 1 serum had antibody against Middelburg virus and 5 against Sindbis virus. A few sera with antibody to Chikungunya virus were found in most of the riverine and coastal localities (all in adults except 2), but not in the 2 mountain groups tested. Antibody to Semliki Forest virus was found only in small numbers of adults from the riverine and coastal areas. Rift Valley fever antibody was found in several sera from both children and adults from riverine localities and in a few sera from coastal areas—the mountain groups were not tested. Only 2 sera [one does not appear in the Table] had antibody to Simbu virus. None of the sera tested had antibody to AR136 virus (isolated from mosquitoes in Tongaland). Only 3 sera from the mountains had antibody to Pongola virus, but there was a high incidence in both adults and children from several riverine and coastal areas. Similarly, antibody to Bunyamwera virus was uncommon in the mountains but common elsewhere in both children and adults. Spondweni antibodies did not occur in the mountains, but a spotty distribution was found elsewhere, mainly in adults. Antibody to Wesselsbron virus was found in 2 of 61 children and 3 of 69 adults from the highlands and infection of domestic animals in this area is thought to occur: antibody was common among both children and adults elsewhere. [The difference in incidence between 2 riverine communities which is discussed does not appear to be significant.] A high incidence of antibody to H336 virus (related to Uganda S virus and isolated from a sick child in Tongaland) was found in several riverine and coastal areas, but not in 2 mountain communities. A significantly higher incidence was found in an area favourable to winter breeding of *Aëdes circumluteolus* than in a nearby area less favourable. Only 4 sera with antibody to West Nile virus were found.

Reference is made to unpublished work demonstrating laboratory transmission of Chikungunya virus by *Aëdes calceatus*.

C. E. Gordon Smith

BEADLE, L. D. **Status of Mosquito-Borne Encephalitis in the United States.** *Pub. Health Rep.* Wash. 1959, Jan., v. 74, No. 1, 84–90, 1 fig. [41 refs.]

This useful paper summarizes the available information on Western and Eastern encephalomyelitis and St. Louis encephalitis, clearly and neatly. Normally these are infections of birds transmitted by mosquitoes and occasionally spilling over to horses, man and other mammals but it is not yet certain how the viruses maintain themselves during the non-epidemic season—possibly by overwintering in mosquitoes, or possibly through a mechanism of recurrent viraemia in birds. The Eastern virus can be transmitted mechanically in pheasants during acts of cannibalism and feather picking, vices common in penned birds.

The author gives the chief mosquito vectors of each virus and shows that vector control may be the most practical approach to prevention. Vaccination is recommended for equines but it is not feasible for man. These viruses are potentially a continuing serious threat for man, and there have been several great epidemics.

Charles Wilcocks

BRODY, J. A. & MURRAY, W. A., Jr. **Arthropod-Borne Encephalitis in the United States, 1957.** *Pub. Health Rep.* Wash. 1959, May, v. 74, No. 5, 461–8, 2 figs.

Human cases of eastern equine encephalomyelitis occurred in Florida and Louisiana. Equine cases in the southern States lasted from May to September and were generally severe clinically. Pheasant infections were uncommon, but occurred in New Jersey and Massachusetts. *Culiseta melanura* has now been recorded biting man in its natural setting.

The majority of human cases of western equine encephalomyelitis were in a single outbreak at Denver, Colorado. More than 100 cases occurred between mid-July and the end of September. Almost half the patients were infants. Equine infections were mainly in an area extending from north-west Utah, through Idaho to western Oregon and Washington. Isolations

from pools of *Culex tarsalis* were made in California, Denver, Greeley (Colorado), Texas, Idaho, North Dakota and Washington. Isolations were also made from *Culex fatigans* in Texas. The virus was isolated from 3 pools of *C. melanura* and 3 times from wild birds in Alabama in October and November.

There was an epidemic of some 119 cases of St. Louis encephalitis in the Rio Grande Valley in Texas. This semi-tropical area, heavily populated with birds, had a long drought after a period of heavy rain. This led to heavy breeding of *C. fatigans*. The cases occurred between mid-July and end of August, the majority being in patients aged 21 to 40 years, but the highest attack rate being in those over 60 years of age. The 3 deaths were all in the latter age-group. There were scattered human cases in California and the virus was isolated from 49 pools of *C. tarsalis* compared with 2 in the previous year. The disease also occurred in Colorado, Missouri and Florida (a new extension of the disease). Isolations were made from *C. tarsalis* in North Dakota, Idaho, Colorado and Washington and from *Culex pipiens* in Kentucky.

C. E. Gordon Smith

GIDDINGS, L. E., SMITH, L. W., BEAVER, Margaret E. N. & SOOTER, C. A. **St. Louis Encephalitis Outbreak during 1956 in Grand Junction, Colo.** *Pub. Health Rep.* Wash. 1959, Apr., v. 74, No. 4, 372–5.

This was the first large outbreak of St. Louis encephalitis in the Rocky Mountains area: there was an estimated attack rate of 162·3 per 100,000 in a city of 18,500 people. 31 cases with no deaths were reported. Cases increased in number from the end of July till late August and ended in mid-October. 3 later encephalitis cases were not apparently due to the St. Louis virus. All age-groups were affected: 42% of the patients were aged between 20 and 39 years. Serum was obtained from 20 of the 31 patients but only 3 were confirmed serologically as St. Louis encephalitis. 13 other patients had suggestive serological evidence of infection.

Serum antibody surveys of 100 human and 103 yearling chicken sera obtained in the area after the outbreak showed 1% with antibody to Western equine encephalomyelitis virus. 16·5% of the chickens and 0–12·5% of the human beings (depending on the test used) showed St. Louis antibody. The incidence of complement-fixing antibody in the human sera varied from 0 to 9% in different age-groups while that of neutralizing antibody varied from 0 to 22%. It seemed likely that most of these antibodies were due to infections acquired before the recent outbreak.

C. E. Gordon Smith

HENDERSON, D. A. & SHELOKOV, A. **Epidemic Neuromyasthenia—Clinical Syndrome?** *New England J. of Med.* 1959, Apr. 9 & 16, v. 260, Nos. 15 & 16, 757–64; 814–18, 1 fig. [43 refs.]

This is an excellent review of the literature on the epidemic disease now known as "epidemic neuromyasthenia" which has, however, been described under various names—"Iceland disease", "benign myalgic encephalomyelitis", "Akureyri disease", "epidemic vegetative neuritis", "acute infective encephalomyelitis", "encephalomyelitis", "persistent myalgia following sore throat", "a disease resembling or simulating poliomyelitis", "atypical poliomyelitis" and "encephalomyelitis resembling poliomyelitis".

Study of the reports "reveals differences among the various epidemics, but most of these concern minor details". The cases have been confined particularly to young and middle-aged adults, and females have been more frequently and severely afflicted. Most notably susceptible have been nurses and physicians. The symptoms have been fatigue, headache, alterations in emotional status, aching muscular pain, paresis and paraesthesias. The clinical course of the disease has been "unaccountably prolonged and debilitating and marked by frequent exacerbations".

There is an account of the history of the disease and a table of "apparent outbreaks of epidemic neuromyasthenia" in many countries ranging in time from an outbreak in 1934 in the United States to one in 1958 in Greece. The largest reported epidemic was in Iceland in 1948–9 where 1,090 cases are known to have occurred in the community.

There is a detailed review of the clinical characteristics of the disease and of its course. Onset is slow and the acute phase lasts for a period of between a few days to several weeks. Resolution is slow and punctuated by exacerbations. Among 198 cases in Los Angeles the average time lost from work was 14 weeks. In a few instances residual symptoms have persisted for months and even years.

The findings of clinical laboratory examinations and of virus and bacteriological studies are described and discussed but no definite aetiology has as yet been determined. The epidemiological features are also considered in some detail. Although deaths "directly attributable to the illness have nowhere been reported" and the "illnesses do not appear numerically important on a national scale" the long-term morbidity among those who are ill and the high incidence in a single outbreak indicate the need for further intensive study of the disease.

M. E. Delafield

FLAX, A. & LEIBOVICI, B. Epidemie hidrică mixtă cu Salmonella typhi, Salmonella para A si bacili dizenterici. [**A mixed Water-borne Epidemic with *Salmonella typhi*, *Salmonella paratyphi A*, and Dysentery Bacilli**] *Microbiol., Parazitol., Epidemiol.* Bucharest. 1958, Nov.–Dec., v. 3, No. 6, 547–50. [11 refs.]

In recent years paratyphoid A has been increasing in the town of Galaţi, Rumania, the cases being associated with the dock area on the Danube where vessels are laid up during the winter. In February 1954 the drinking water supply froze and men working in the dock area used water from the dock basin for all purposes. An epidemic then broke out which involved 8% of the total population at risk; 58 cases of mixed typhoid-paratyphoid infection and 2 cases of *Shigella flexneri* infection were observed.

D. J. Bauer

MANCHANDA, S. S., SINGH, H. & CHITKARA, N. L. **Enteric Fever in Children. (Review of 270 Cases.)** *Indian J. Child Health.* 1959, June, v. 8, No. 6, 273–80. [12 refs.]

This paper reviews the clinical aspects of enteric fever in a series of 270 children admitted to hospital in Amritsar, East Punjab, India, between 1955 and 1959. The diagnosis was confirmed in each case by isolation of the organism or by the demonstration of a rising agglutination titre.

Admissions for enteric fever were twice as frequent in the hot months of May to October as during the rest of the year. The youngest patient was 9 months old, 87 were below the age of 5 years and 134 between 5 and 10 years; 17 were below the age of 2 years. Males outnumbered females by 2 to 1.

The clinical features, which are tabulated, show that cough (incidence 27·8%) was rather less frequent than would be expected in a group of adult patients, and the occurrence of a rash (1·86%) far less frequent. Abdominal symptoms, however, were rather more common, the frequency of their occurrence being as follows: diarrhoea, 18·5%, constipation, 14·4%, meteorism, 9·6%, vomiting, 12·9%. Meningismus was shown by 12 patients (4·44%), though the cerebrospinal fluid was normal in each case. Convulsions occurred in 3 children and stupor or coma was shown by 55 (20·3%) on admission. The spleen became palpable in 57 (21%).

Positive blood cultures were obtained in 62 (38·8%) of the 160 attempts made, the percentage of positive results during the 1st, 2nd, 3rd, 4th and subsequent weeks being 53·3, 37·3, 29·6, 14·3, and 12·5 respectively. [This measure should be taken, therefore, in every suspected typhoid patient, however late in the disease he may be received.] The Widal reaction provided valuable confirmatory evidence, the titre to the O antigen rising to more than 1/250 in 239 patients. Leucocyte counts were not helpful, since only 21·9% of patients showed a characteristic leucopenia of less than 5,000 per cmm.

Treatment was by chloramphenicol, at a dosage of 50 mgm. per kgm. body weight per day, in divided doses given every 6 hours. An initial loading dose equal to one-half the total daily dose was employed. The dose of the antibiotic was tapered off in 4–6 days after defervescence. Prednisolone was given in 14 instances of particular virulence, including 3 children with intestinal perforation: though all the latter died the steroid appeared to have swung the balance in favour of all the others.

5 children were admitted with intestinal perforation; all were treated conservatively on conventional lines but all died. [This cannot be wondered at, for all must have developed extensive peritonitis before coming under treatment.]

[This account illustrates the well-known divergence of the picture of enteric fever in children from the classical description based on the disease as seen in adults.]

J. H. Walters

MACCIOTTA, A. & CHIAPPE, F. Osservazioni sulla funzionalità epatica nell'infezione tifoide dell'infanzia. **[Liver Function in Children suffering from Typhoid Fever]** *Arch. Ital. Sci. Med. Trop. e Parassit.* 1959, June, v. 40, No. 6, 297–318. [44 refs.] English summary.

In 1958 the authors having examined 60 children suffering from typhoid never found evidence of hepatitis or hepatic insufficiency though on the other hand liver enlargement, usually painless and not marked, was constant. They then performed a number of biochemical tests of liver function on 10 children aged between 2 and 11 years, the tests being carried out both in the acute and convalescent stages. No less than 10 different tests were performed on the blood, *e.g.* alkaline phosphatase, transaminases, protein electrophoresis, direct and indirect bilirubin, etc. and in addition urinary urobilin and bile salts were investigated. The results are summarized in a table.

They are rather surprising as on the whole they showed only minor variations from the accepted norms and all returned to normal on convalescence.

The authors consider that in the acute phase there is evidence of damage to the liver cells, though the mesenchymal components are also affected and though changes are slight; the relation of the esterified cholesterol to Koller's test (prothrombin after vitamin K loading) and the two serum transaminases (glutamic-oxalacetic, and glutamic-pyruvic) are regarded as the best indices.

[It is not clear whether these 10 cases were all due to *Salmonella typhi*.]

W. K. Dunscombe

HENDERSON, N. D., GARLOCK, F. C. & OLSON, B. H. **Treatment of Acute Typhoid with Synnematin B. Report of a Case.** *J. Amer. Med. Ass.* 1959, Apr. 25, v. 169, No. 17, 1991–4, 1 graph.

The use of the antibiotic synnematin B in the treatment of typhoid fever was reported in 16 cases by BENAVIDES *et al.* [this *Bulletin*, 1955, v. 30, 956]. This drug gave results comparable to those with chloramphenicol except that no carriers have yet been reported after synnematin B treatment; the drug is believed to be bactericidal in adequate dosage [*ibid.*, 1958, v. 33, 1075]. The present report does not, unfortunately, carry the matter any further. It describes a case in which chloramphenicol was given for 3 days and produced no improvement; but the dosage was only 1 gm. daily for the first day, and is not stated for the subsequent days. Synnematin B was then given intramuscularly every 4 hours in daily dosage of 80,000 units per kgm. for some 3 weeks. After 48 hours the patient improved but the temperature did not become normal for over 2 weeks. [No conclusion can be reached about either antibiotic from this report.]

H. Stanley Banks

SCHUBERT, J. H., EDWARDS, P. R. & RAMSEY, Carolyn H. **Detection of Typhoid Carriers by Agglutination Tests.** *J. Bacteriology.* 1959, May, v. 77, No. 5, 648–54. [16 refs.]

Although Vi-agglutinins were demonstrated in the serum of a typhoid carrier in 1935 by FELIX *et al.* [*J. Hygiene*, 1935, v. 35, 421; this *Bulletin*, 1936, v. 11,

(71)] the technical difficulties of recognizing Vi-agglutination with a living culture of the typhoid bacillus containing H, O and Vi antigens were too great for the test to be widely used. When, however, the typhoid strain "Vi I" [BHATNAGAR *et al.*, this *Bulletin*, 1939, v. 14, 342] became available the test was much simplified. This strain was rich in Vi but deficient in H and O antigen and did not react to H and O antibody and could be used as a formolized suspension. Nevertheless, the instability of the strain—S-R variation due to its deficiency in O antigen—was a disadvantage.

The preparation of a standardized Vi suspension was a tedious and exacting procedure but within a few months of the availability of the Vi I strain it was found possible to prepare a Vi suspension for routine use that gave reliable results so long as the test was controlled by the inclusion of a standard Vi serum. [The reviewer was closely connected with this work from its very inception until recent times and although, in his opinion, the test was of great value in indicating the possibility of a carrier condition, the frequency of low Vi titres in known carriers made the interpretation of the results no easy matter unless full standardization technique was observed. Felix, himself, fully appreciated the disadvantages of the test and he never made extravagant claims; he presented the exact records of his experiments and was extremely critical of other work where similar controls were not observed.]

Since that time an extensive literature has accumulated on the value of the Vi test for the detection of typhoid carriers. All the papers were not of equal standard and many reports were of a conflicting nature. When the haemagglutination test was introduced for the estimation of Vi-antibody Felix, after due consideration, felt that while the increased sensitivity was an asset there was insufficient evidence to show that the specificity of this more complicated test was any greater than the simple Vi bacillary agglutination test. The Vi haemagglutination test has, however, gained favour with other workers and the paper by the present authors compares the results of the standard Vi tube agglutination test employing the Vi-antigen prepared by the Standards Laboratory of the Public Health Laboratory Service, London, the Vi slide agglutination test of SAINT-MARTIN and DESRANLEAU [*ibid.*, 1951, v. 26, 1058] and a modified form of the Vi-haemagglutination test of LANDY & LAMB [*ibid.*, 1953, v. 28, 855]. As far as possible the specifications and recommendations of the authors of the respective tests were followed throughout. The tests were performed on the sera of 180 known typhoid carriers and the sera of 200 healthy persons without a history of typhoid. Not one of the control sera showed Vi antibody and over 90% of the carrier sera were positive by the haemagglutination test and about 65% with the bacillary tube agglutination test; the slide test gave results which fell between these two figures.

Other workers have obtained similar results with the haemagglutination test but this paper has particular interest because of the complete absence of any false positives with any of the three methods employed and the care taken in comparing the three techniques. Although the haemagglutination test, used alone, failed to demonstrate Vi antibody in about 10% of the carriers, when all three methods were used the failure was reduced to less than 1%. *H. J. Bensted*

JERSILD, T., NEUKIRCH, E., RAUN, J., RIWERTS-ERIKSEN, K. & TULINIUS, S. **Typhoid Carriers treated with High Dosages of Penicillin.** *Antibiotic Med.* New York. 1959, May, v. 6, No. 5, 292–4.

The authors treated 8 typhoid carriers with penicillin, 2 million units 3 times daily: 7 had the treatment for 3 weeks, the other for only 10 days. 4 patients remained carriers after the 3-week course; all had cholelithiasis. Of the other 4, 3 were cured after the 3 week course: none of them had cholelithiasis. The remaining patient was first treated with chloramphenicol: his stool tests remained positive during treatment, but when treatment was changed to penicillin tests became negative and remained so, though penicillin was given for only 10 days. It is suggested that the bacteriostatic effect of chloramphenicol followed immediately by the bactericidal effect of penicillin may have been responsible for the favourable outcome in this case. Of the patients treated 7 had been carriers for 3 to 32 years, the remaining patient for 9 months. From those cured between 24 and 72 stool tests had been negative. *A. B. Christie*

BERGSMA, C. Veterinaire problemen bij de epidemiologie der Salmonellosen. **[Veterinary Problems concerning the Epidemiology of Salmonellosis]** *Tijdschr. v. Diergeneesk.* 1959, Aug. 15, v. 84, No. 16, 872–91. [37 refs.]

"Attention is drawn to the marked increase in the incidence of infections due to *Salmonella* in man and animals both in the Netherlands and in other countries, with the exception of the more unipathogenic human types *S. typhi murium* and *S. para-typhi B*, the incidence of infections caused by these types in Western Europe presenting the reverse picture.

"Other types are constantly being identified and the incidence of family infections and sporadic cases shows a particularly marked increase. The causes of this high morbidity rate are studied. In addition to known sources of infection (inter al., rodents, pigeons, ducks and flies), special attention is drawn to the altered methods of cattle-feeding in the post-war period, animal products (animal-, bone-, blood- and fish-meal, egg products) frequently from other countries and often infected with *Salmonella*, having been substituted for a part of the feeding-corn.

"As this altered method of feeding has been mainly adopted in the case of poultry and pigs, this is one of the principal reasons why poultry and pigs are the chief reservoir of *Salmonella* to-day. This increasing incidence of infections in man and animals has also attracted considerable attention in other countries. Especially imported cattle-food products are in ill repute and in countries such as Denmark and Germany legal measures have been adopted to eliminate this source of infection.

"In neighbouring countries, *Salmonella* was frequently isolated from egg-products imported from the

Netherlands. If Holland is to retain its leading position in the export-market, no time should be lost in adopting radical measures directed towards safeguarding animal products obtained in the Netherlands as well as products imported from other countries, which are intended for man and animals, from infection with *Salmonella*.

"This is a veterinary health problem of the first order, of vital importance both to producers (owners of live-stock) and consumers. Some lines of action which may contribute towards achieving the desired aim are indicated."

JOHNSON, R. & LANDSMAN, Joan B. **Antibiotic Treatment in Dysentery.** *Scottish Med. J.* Glasgow. 1957, Oct., v. 2, No. 10, 383–8.

479 patients suffering from Sonne or Flexner dysentery were treated with varying doses of chlortetracycline, oxytetracycline, chloramphenicol, polymyxin, neomycin and sulphadiazine or streptomycin and sulphaguanidine. Chlortetracycline and oxytetracycline seemed the most effective treatment with a combined total failure rate of only 2·2%. Even when the dose of oxytetracycline was only 5 mgm./kgm. body weight per day the failure rate was only 4·1%. Chloramphenicol had a failure rate of 16·6%, neomycin and sulphadiazine 27·3%, and streptomycin and sulphaguanidine 26·4%. The dosage of streptomycin was only 0·5 gm. per day although much higher oral dosage can be given without any side effects. Chlortetracycline, on the other hand, produced side effects in 15·4% of patients, and oxytetracycline in 8%, although in dosage of 10 mgm./kgm. body weight per day side effects occurred in only 3·3%. The authors feel that oxytetracycline is the best drug to use.

A. B. Christie

TAYLOR, P. J. **Acute Bacillary Dysentery in Cyprus. A Comparative Study of Treatment in 332 Cases.** *Brit. Med. J.* 1959, July 4, 9–12, 1 chart. [16 refs.]

Although sulphonamides have been the standard therapeutic agents in bacillary dysentery for the past 20 years, certain controlled trials carried out during the period 1944–6 had thrown doubt upon their efficiency. In the Korean war the broad-spectrum antibiotics proved effective [this *Bulletin*, 1953, v. 28, 794]; their use, however, may be attended by the risk of serious side effects in a small proportion of patients. Oral streptomycin, and a combination of sulphonamides and streptomycin have also been advocated.

The author, faced with such a diversity of therapeutic choice, decided to carry out 2 controlled trials on service patients admitted to the RAF Hospital at Akrotiri, Cyprus. The first trial, which took place in 1957, tested the relative efficiency of phthalyl sulphathiazole against the results obtained by purely supportive therapy together with inert dummy tablets. The second trial, in 1958, compared the results of the same course of phthalyl sulphathiazole with those obtained by the use of a combined tablet containing a mixture of 3 soluble sulphonamides together with streptomycin.

The subjects were all young Servicemen aged 19 to 30 years, all of whom were received in the wards within 48 hours of the onset of their disease. The diagnostic measures employed comprised the examination of 3 daily consecutive stool specimens by microscopy, for the recognition of the characteristic "bacillary exudate", and by culture on desoxycholate citrate agar, any resulting colonies being identified by slide agglutination and sugar reactions.

The shigellae isolated from 146 patients during the 2 trial years comprised:

Sh. flexneri	1	12·3%
„	3	1·4%
„	6	35·6%
Sh. sonnei		49·3%
Sh. boydii	3	1·4%

It is of interest to note that the bacteriology of acute bacillary dysentery in the Eastern Mediterranean area appears to have changed since the end of World War II, when BOYD [this *Bulletin*, 1946, v. 21, 851] reporting the isolations from 27,414 men of the Middle East Forces 1940–1943, noted the following incidences: *Shigella dysenteriae* 1 19%, *Sh. dysenteriae* 2 7%, *Sh. flexneri* 62% and *Sh. sonnei* 7%. Thus the disease, in Cyprus at least, appears to have become more benign.

In the first trial phthalyl sulphathiazole was used in the heavy RAF standard dosage, *viz.* 9 gm. initially, followed by 4 gm. 5 times daily for 6 days. The control group received dummy tables containing mixed vitamins in homopathic doses, twice daily. Each group received Mist. kaolin et morph. B.P. as often as required. The clinical impression gained from this first trial was that diarrhoea and discomfort subsided about 24 hours earlier in the sulphonamide than in the control group. The ability of either form of treatment to abolish the infection completely was examined by culture of stool specimens daily for 6 days from the second day after the completion of treatment. In the sulphonamide group the incidence of bacteriologically-proved relapse was 3·3% and of clinical relapse 8·6%, but in the control group a significantly higher relapse-rate obtained, corresponding figures being 20% and 15·6%.

In the second, larger experiment, alternate patients were assigned to a group receiving an identical course of phthalyl sulphathiazole or to a second group which received tablets of Streptotriad, 3 tablets thrice daily for 6 days. Each tablet of Streptotriad contained streptomycin 65 mgm., sulphathiazole 100 mgm., sulphadiazine 100 mgm., and sulphamerazine 65 mgm.

Clinical effectiveness of each form of therapy was judged by the duration of diarrhoea (defined as the passage of more that 2 loose stools daily) from the beginning of treatment. In the phthalyl sulphathiazole group this was 3·45 days in the bacteriologically proved cases, 3·43 days in the "clinical" cases, with a mean for the whole group of 3·44 days. In the Streptotriad group corresponding figures were 2·84, 3·02 and 2·95 days. These differences, though small, were

statistically significant. The relapse rates in the sulphathiazole group were 8·9% and 8·6% for the bacteriologically proved and "clinical" cases respectively, and in the Streptotriad group 10·8% and 4·8%. These results showed no statistically significant difference.

This well conducted trial shows that in the mild type of bacillary dysentery prevailing in Cyprus chemotherapy with heavy doses of an insoluble sulphonamide gives better results than symptomatic treatment alone, while a combination of streptomycin and 3 soluble sulphonamides is more beneficial still. The last form of treatment has the advantage for a patient who may be nauseated that the bulk required to be swallowed is far less than that implied by the standard RAF course of phthalyl sulphathiazole. *J. H. Walters*

Falisevac, J., Kosutic, Z. & Galinovic-Weisglass, M. **Sulphonamides and Streptomycin in Bacillary Dysentery. A Controlled Trial.** *Brit. Med. J.* 1959, July 4, 12–13.

This paper, from Zagreb, records the results of a clinical trial in bacillary dysentery of soluble sulphonamides alone, sulphonamides and oral streptomycin, and streptomycin alone. The practical considerations providing the motive for this experiment were the increasing frequency of sulphonamide-resistant strains of *Shigella sonnei*, the expense of streptomycin and the occasional discovery of shigella strains resistant to it, and the prohibitive cost and risk of dangerous side effects implicit in the use of the tetracyclines. The 3 experimental groups were roughly [but certainly not strictly] comparable in the age composition, duration of disease before treatment and distribution of shigella types. Each contained examples of *Sh. flexneri* and *Sh. sonnei* infections, together with clinical cases from whom no isolations were made, while *Sh. dysenteriae* 2 and *Sh. boydii* 7 were represented in 1 group each.

The courses of treatment under trial were as follows:—

Group 1. Sulphatriad 1 gm. every 6 hours for 7 days. (Sulphatriad contains sulphathiazole 0·185 gm., sulphadiazine 0·185 gm. and sulphamerazine 0·130 gm. in each tablet of 0·5 gm.)

Group 2. Streptotriad 2 tablets every 6 hours for 4 days (each tablet containing 65 mgm. of streptomycin sulphate and 265 mgm. of Sulphatriad).

Group 3. Streptomycin tablets of 250 mgm.: 2 every 6 hours for 4 days only.

The dosages refer to adult patients, proportionate reductions being made for children. A control group treated symptomatically was planned but abandoned since the first 2 patients remained ill for a long time.

[The small numbers of patients in each group, 12, 15 and 21 respectively, and the heterogeneity of the group, preclude any statistical analysis of the results obtained, but a clinical assessment of their relative value is given below.]

The results obtained with Sulphatriad alone were fairly satisfactory, all patients being free from symptoms by the 6th day and bacteriologically cured by the 5th day, though *Sh. sonnei* persisted longer than *Sh. flexneri*.

Streptotriad gave comparably prompt relief of symptoms but a more rapid elimination of the causal organism in most patients, with the exception of 3 with *Sh. flexneri* infection, one of whom required a subsequent course of chloramphenicol.

Streptomycin alone proved surprisingly disappointing both in its symptomatic and bacteriological effects: 3 *Sh. flexneri* infections remained positive until the 5th, 6th and 7th days respectively, while some patients with *Sh. sonnei* disease were still infected on the 7th day.

[This paper is of value in confirming the therapeutic efficiency of a mixture of streptomycin in small doses with soluble sulphonamides in the treatment of bacillary dysentery.] *J. H. Walters*

TUBERCULOSIS

Karns, J. R. **Tuberculosis in Medical Students at University of Maryland.** *Amer. Rev. Tuberculosis.* 1959, June, v. 79, No. 6, 746–55, 2 figs. [14 refs.]

This report presents the experience with the student body in the medical school of the University of Maryland from 1934 to 1957 in regard to the trend of tuberculin sensitivity and the attack-rate of clinical tuberculosis during attendance at the school.

The number of students adequately studied was 2,302. More than 90% were tuberculin tested at entry and all were X-rayed. Periodic tuberculin testing of non-reactors and X-ray examination of all students were done throughout the medical course. There was no programme of BCG vaccination; the few individual students who were vaccinated on their own initiative were insufficient to affect the statistical results of the study.

The reactor rate of entrants in 1934 was 65·4% and in 1957 10·6%. The annual conversion rate was about the same throughout the period. The number of non-reactors who converted annually gives a true picture of the incidence of infection for each year. There was little difference in conversion rates until 1950–4 when they were definitely lower for each year than in any earlier groups, ranging from 3·7% for junior to 7·4% for senior students.

In 1934–9 and 1940–4 third-year students had the highest conversion rates, in 1945–9 second-year students, but in 1950–4 there was no significant difference between any of the years.

17 students developed tuberculosis during the 23 years of the study; 16 were discovered in 1934–49 and only 1 since 1950. Details of tuberculin state on entry, conversion, date of diagnosis and clinical features are presented. Of special interest was the development of pulmonary tuberculosis after a tuberculous chancre acquired during an autopsy examination.

5 of 875 reactors (5·71 per 1,000), and 12 of 1,427 non-reactors (8·4 per 1,000) developed pulmonary

tuberculosis. In 5 cases the first appearance of tuberculin sensitivity and radiological evidence of the disease were found simultaneously; 10 students presented evidence of tuberculosis within 6 months of the demonstration of tuberculin conversion.

In the group of non-reactors at entry pleurisy with apical infiltration was found in 1, minimal pulmonary disease in 10 and moderately advanced disease in 1. In original reactors there was minimal disease in 3 and moderately advanced disease in 2. There was 1 death in the series.

The recent low morbidity reported was achieved without the use of BCG vaccination. It is attributed to early diagnosis and treatment, improved methods of treatment and management of tuberculosis as a contagious disease. The author remarks that medical students still run a greater risk of tuberculous infection than other students and continued vigilance is still necessary. *H. G. Calwell*

GÓMEZ, F. D. & RACINE, R. Estudios sobre alergia tuberculinica en estudiantes universitarios. Modalidades y variaciones en relación al riesgo de contagio. **[Tuberculin Allergy in University Students: Changes in relation to Risk of Infection]** *Hoja Tisiológica.* Montevideo. 1958, Dec., v. 18, No. 4, 248–58, 298–9, 1 chart. English summary.

The following is a translation of the authors' conclusions:—

"An analysis of the course of tuberculin allergy during the period of study in the respective Faculties [of the University of Montevideo] of 3,046 students (1,519 of medicine, 1,527 of law) indicates that:—

"1. On entry to the respective Faculties almost one-half were positive to 1,000 TU.

"2. In four-fifths the reaction was slight.

"3. A greater tendency to increase in sensitivity to tuberculin was observed in the medical students than in the others.

"4. The proportion of conversions was 35·1% higher in the medical students than in the others.

"5. The investigations indicate a serious risk of infection in medical students." *Charles Wilcocks*

BOGEN, E. **Postmortem Transmission of Tuberculosis.** *Amer. J. Clin. Path.* 1959, Apr., v. 31, No. 4, 343–4. [14 refs.]

The author begins this short paper with a discussion of published work on the risk of infection in laboratory or autopsy workers in contact with tuberculous material, and he gives a useful list of references. At his own hospital, Olive View Sanatorium, California, guineapigs have for 12 years been kept in an open cage near the autopsy table, and on 3 occasions have been found infected, with lesions chiefly in the lungs. On each occasion a fault in technique could be recalled which would account for the infection. Great precautions are taken to protect the pathologist and his assistants or visitors, especially where abscesses and collections of fluid are being opened. These precautions involve the use of gowns, gloves, masks, caps, coverings for the corpse and Cellophane or paper sheets for use as shields where abscesses are opened. A special table has been devised for the handling of tuberculous animals, with a pane of glass between the animal and the operator, and surgically resected specimens are examined in a bacteriological hood. The subject is important. *Charles Wilcocks*

MUNTENDAM, P. **The Influence of the Social Milieu on the Manifestation and Course of Tuberculosis.** *Acta Tuberculosea Scandinavica.* 1959, v. 37, Nos. 1/2, 63–88, 8 figs.

This is the third of the scientific papers read before the Netherlands Society of Chest Physicians. The author's intention was to remind his audience that environmental influences are still of the greatest importance in the fight against tuberculosis.

The relationship between housing and tuberculosis is discussed and evidence brought forward of the effect of poor accommodation and overcrowding. Increased risk of infection in such an environment is beyond doubt but its effect on the development of the disease in infected persons is less clear.

Because of the absence of statistical proof of a connexion between bad housing and tuberculosis Muntendam obtained an analysis of the incidence of new cases (including relapses) of tuberculosis in Holland in the period 1952–6. It was deduced from the figures that the overcrowded dwelling promotes familial infection. Extra-familial infection is, however, not clearly influenced by the standard of housing. The incidence of unknown sources of infection was highest in those who were housed best.

Muntendam does not doubt the possibility of the influence of psychological factors on the pathogenesis of tuberculosis but he does not find it proven and advises caution in attributing a direct relationship to such factors.

The infection of secondary schoolchildren, when extra-familial, is usually caused by another pupil. Periodical tuberculin testing of schoolchildren and X-ray examination of reactors is therefore advisable.

Tuberculosis as an occupational disease is still commonest in nurses in sanatoria and, in descending order, in general hospitals with a tuberculosis department, mental hospitals and general hospitals without a tuberculosis department. The incidence of the disease in nurses is declining because of improvement in their working conditions and the application of preventive methods including BCG vaccination.

It is stressed that even where tuberculosis does not occur as an occupational disease the working environment should be so regulated that if a source of infection arises spread will be controlled. Periodical examinations should be made in all industries in which young workers are employed. The closest collaboration between clinics, the industrial medical service, the labour inspectorate and the medical officer of health should be maintained.

The influence of industrialization is no longer of great moment in western Europe but it is still of importance in countries which are being developed.

The relationship between nutrition and tuberculosis requires epidemiological, laboratory and clinical study. The author believes that malnutrition is the most important external factor connected with the manifestation of the disease. The fact of the connexion is established but its mechanism is still not clear.

Special attention must be paid to the health and environment of immigrants, especially those from the tropics who are often overcrowded, and to social misfits such as alcohol addicts. *H. G. Calwell*

DUBOS, R. J. **The Host in Tuberculosis.** *Acta Tuberculosea Scandinavica.* 1959, v. 37, Nos. 1/2, 42–60. [45 refs.] Discussion 60–62.

This paper also was read to the Netherlands Society of Chest Physicians.

Tuberculosis has long been recognized as a social disease, most prevalent in the economically underprivileged and characteristic of certain phases of civilization. Around 1850 the death rate from tuberculosis in the cities of Europe and America was about 500 per 100,000; in 1900 it had fallen to about 200; and in 1945, before the advent of chemotherapy, it was 50 or less in spite of the almost universal prevalence of infection as judged by reactor rates in adults.

There is evidence that the character of the disease has changed with time and in different people at different times and in different stages of civilization. There is, however, no evidence to support the hypothesis that the tubercle bacillus has suffered some loss of virulence. The survival and multiplication of people with a higher than average resistance to infection has led to the evolution of more resistant stock.

In addition to heredity environment plays a large part in conditioning the outcome of infection not only by influencing the chance of it occurring but also by determining its outcome. The two World Wars provided human experiments illustrating this. At the outbreak of each tuberculosis mortality was declining fairly steadily but it began to increase immediately. As soon as peace was restored the favourable trend was resumed.

Malnutrition is one of the main factors in the increase in tuberculosis during social upheavals. Experiments carried out in recent years leave no doubt that resistance to the infection can be decreased by deficiencies in certain vitamins, fats and proteins even if they are not such as markedly to affect the weight and condition of control animals. Mice fed on diets complete except for casein deficiency were more susceptible to experimental tuberculosis than were mice receiving the same diet with more casein. The addition of essential amino-acids corrected the infection-enhancing effect of the low casein diet. The quality of the protein was also found to be as important as its quantity. Dubos remarks that these experimental findings may not be applicable to human tuberculosis.

Little is known about the mechanism of acquired resistance. There is no evidence that allergy to tuberculin and immunity are interdependent.

The activation of arrested tuberculous lesions has been attributed to many factors such as malnutrition, fatigue, strain, uncontrolled diabetes or cortisone. Examples are given of many physiological, biochemical, social and emotional factors that might influence the tubercle bacillus within the host or the histopathological character or the tuberculous lesion.

The conclusion drawn is that the use of chemotherapy does not mean the conquest of tuberculosis. Some at least of the successfully treated patients will relapse and again become infectors. Countless numbers are already infected and many will develop tuberculosis if the equilibrium between host and bacillus is upset. How to maintain this equilibrium demands continuous study. *H. G. Calwell*

ENTERLINE, P. E. & KORDAN, B. **A controlled Evaluation of Mass Surveys for Tuberculosis and Heart Disease.** *Pub. Health Rep.* Wash. 1958, Oct., v. 73, No. 10, 867–75, 2 figs.

A certain proportion of X-ray films of the chest are always differently interpreted by two readers, however similar their training. The authors have used this phenomenon of "observer variability" to assess the value of large-scale surveys of tuberculosis and heart disease. 200,000 films, from 2 surveys in Dallas and Los Angeles counties, were re-read $2\frac{1}{2}$–$4\frac{1}{2}$ years later by physicians of camparable standing to those who interpreted the original films. The study group consisted of those cases originally reported as positive, and therefore given the benefits of case-finding, and negative at reassessment. The control group consisted of those cases originally returned as negative and therefore untreated, who were subsequently reported as positive. Cases were, however, only included in both study and control groups if considered positive by the second author, a radiologist. The mortality of 3,179 study cases and 2,722 control cases was followed up for a period of 2–3 years from the vital statistics records of each State. The mortality of the study group was less than that of the control group, although it contained a higher proportion of cases considered to be active. The age-sex-race-adjusted death-rate of the study group was 3·13 per 100 for the whole period of follow-up, about one-third lower than the comparable rate of 4·73 per 100 for the control group. This difference is significant at the 5% level at each of 3 broad age-groups. The excess of mortality in the control group was almost entirely accounted for by deaths certified as cardiovascular, chiefly by those due to arteriosclerotic heart disease. Only one death in the study group was certified as due to tuberculosis, and no deaths were so certified in the control group.

Cases thought at the original survey or at reassessment to show a cardiovascular abnormality were studied in the same way. The control group showed a higher mortality at each age, but in no case was the difference significant.

Possible sources of bias, which might have influenced the results, are considered, such as a greater tendency of those in the study group to change their residence to another State. This was, however, discounted by comparing in each group mortality in the first year after the survey, which would be reported back to the State where the survey occurred. In the case of both

the tuberculosis suspects and the cardiovascular suspects, about the same number of deaths were reported in the first year as in the subsequent years of follow-up.

The differences between the study group and the control group are considered to be rough estimates of the benefits of community chest X-ray surveys.

A. S. Fairbairn

COCHRAN, J. B., FLETCHER, W. B. & CLAYSON, C. **An Experiment in Mass Radiography.** *Brit. Med. J.* 1959, July 4, 1–5, 5 figs.

From March to July 1957 a mass radiography survey was made in the market town of Dumfries in south-west Scotland (population 26,683). The survey was designed primarily as a controlled experiment to measure the influence of a preliminary census and of home-visiting on the response of the population. A further aim was to compare the prevalence of pulmonary tuberculosis in the town with that discovered in a neighbouring rural area in 1956 [this *Bulletin*, 1957, v. 32, 1,037].

The town was divided into 3 sectors which were treated differently as follows: A, preliminary census, home-visiting and general propaganda; B, census and general propaganda; C, general propaganda with a census after the completion of the survey.

The total number of inhabitants aged 15 years and over resident at home during the census was 20,269 of whom 14,136 (69·7%) were X-rayed. The response in sector A was 87·6%, in sector B 64·5% and in sector C 64·3%. Home-visiting increased the response by 20% up to the middle-age groups and thereafter by about 30–40%. There was evidence that the personal contact of a census also increased the response of the elderly.

Information was obtained from all those who were X-rayed regarding previous chest X-ray examinations. 40% of males and over 50% of females had not been X-rayed previously. Even in the age-group 15–24 years 40% had not been X-rayed before.

The population in sector A (4,679) which was intensively visited was used to obtain information about response to mass radiography survey and reasons for not attending. Tenants of publicly owned houses responded slightly better than the others (91·2% compared with 86·7%). At age 65 and over there was no difference in the response rates in these 2 groups.

Approximately 10% of those not X-rayed were physically unfit at attend the unit. A further 15% had legitimate health reasons for not attending although fit to attend. About 15% had been X-rayed recently but not within 6 months of the start of the present survey. The remaining 60% had no clear reason for refusing. Over the age of 65 the proportion of those physically unfit to attend was 3 times greater in women than in men.

21 new cases of active pulmonary tuberculosis were discovered (1·5 per 1,000 X-rayed). 8 of the 10 female patients were under 45 while 7 of the 11 new male patients were over 45. The pattern was similar to that found in the rural area the previous year.

In the year after the completion of the survey 12 additional cases of active pulmonary tuberculosis were notified; 9 of these new patients had not been X-rayed in the survey. None was from the sector where home visitation had been done (response 86%); this shows the value of a high response rate. 5 of the 9 patients were over 65 years of age, whereas in the survey no active disease was found above that age. The residue of tuberculous infection appeared to be in the areas and at the ages where the response was least satisfactory.

H. G. Calwell

MEISSNER, Gertrud. Der Einfluss des Bazillus auf den Ablauf der Tuberkulose. **[The Influence of the Bacillus on the Course of Tuberculosis]** *Acta Tuberculosea Scandinavica.* 1959, v. 37, Nos. 1/2, 5–36, 28 figs. [32 refs.] Discussion 37–41.

This paper was read before the Netherlands Society of Chest Physicians at their Jubilee meeting.

Various mycobacteria possess pathogenicity of varying degree according to their ability to invade tissue, to multiply and spread and to form foci of disease.

The most exact method of assessing the virulence of a strain of tubercle bacillus is by controlled experiment in guineapigs. The animals are killed 2–3 months after infection, the extent of the lesions is recorded and an index of the organism's pathogenicity obtained.

Assessed thus in animals infected subcutaneously the bovine strain of tubercle bacillus was found to be the most virulent for guineapigs (index 13), the normal human type less virulent (10·9), an isoniazid-resistant strain of human type less virulent still (2·4) and the avian type produced lesions which were assessed at 2·1. An atypical photochromogenic strain gave an index of 0·7, and other atypical strains, saprophytes and BCG were found to be almost non-pathogenic in guineapigs.

The paper records many details of the result of inoculating the animals intravenously. Some differences were found in the course of the ensuing disease compared with that following subcutaneous infection.

The death of the bacilli in the animal's tissues is an expression of reduced virulence. Isoniazid-resistant bacilli belong to the group whose virulence is reduced but they show the highest degree of pathogenicity within the group. Causes of impaired virulence are discussed; it may be due to the action of the host's tissues, to mutation or to the effect of drugs on the metabolism of the bacillus.

Resistant strains emerging during treatment with isoniazid have diminished vitality. Details of their behaviour in culture are given. Their loss of virulence modifies the course of the disease in guineapigs so that there is less generalization of lesions and regressive changes are seen.

Studies of the constancy of isoniazid-resistant strains, catalase negativity and impairment of virulence showed that these characteristics were hereditary and persisted through repeated passages.

The rest of the paper deals with the behaviour of tuberculosis in man when the causative organism is resistant to isoniazid and so of diminished virulence. Loss of virulence could lead to reduction in infectivity and to less serious disease in an infected person. Primary infection with isoniazid-resistant bacilli has

been reported in varying proportions. In 1953–7 2·4% of 3,915 patients yielded tubercle bacilli which showed primary isoniazid resistance. There is evidence that the incidence is decreasing.

The course of the disease in persons infected with such a strain is not absolutely comparable with that in experimental animals. There are reports that adults infected with organisms primarily resistant to isoniazid (and of impaired virulence) fare better than those whose bacilli are resistant to streptomycin or PAS, if the disease has been discovered early. When the disease is discovered late the response is less favourable.

The favourable result seen experimentally is more difficult of attainment in man because of the poor state of resistance generally present in patients in whom drug resistance of the bacillus has occurred and the consequent development of forms of tuberculosis which rarely occur in animals and whose course in them is not known.

Both adults and children infected by primarily isoniazid-resistant bacilli have a good prospect of recovery. Resistant strains can be found in resected tissue and when they are present there is histological evidence of an active healing process. They are, however, found also in old advanced cavitary lesions, but even patients with advanced disease who continue to be treated with isoniazid are not likely to die of tuberculosis but of some intercurrent condition.

H. G. Calwell

Shah, J. R., Warawadekar, M. S., Deshmukh, P. A. & Phutane, P. N. **Institutional Survey of Pulmonary Tuberculosis with special reference to Smoking Habits.** *Indian J. Med. Sci.* 1959, May, v. 13, No. 5, 381–92, 2 diagrams. [13 refs.]

In the course of an investigation into social habits and tuberculosis in Bombay, 439 male employees of the Haffkine Institute were questioned about their smoking habits and submitted to mass X-ray examination. This, with a fuller examination in doubtful cases, produced 46 individuals who were considered to have pulmonary tuberculosis, of whom 17 were active, and 29 quiescent; the age-groups are given. The authors report that the patients diagnosed as having tuberculosis were 10·48% of the total; 8·29% were smokers and 2·28% non-smokers. The incidence of smokers in the 439 subjects was 57·18%, but only 13% of these smoked more than 10 cigarettes a day. The difference between the incidence of tuberculosis in smokers and non-smokers is thought to be statistically significant.

F. H. Young

Spangberg, J. **A Clinical Study of the Haemagglutination Reaction in Tuberculosis.** *Acta Tuberculosea Scandinavica.* 1959, Suppl. 46, 96 pp. [Numerous refs.]

This extensive investigation was carried out at the University Hospital, Uppsala, and the experimental work was done on the sera of a large number of patients and normal subjects. It is presented in the form of a monograph; the introduction, which is extensive and well documented, reviews the various cells and antigens that have been used in the test, the cross-reactions that occur with other antigens, the use of the test in veterinary medicine, the effects of tuberculin testing and BCG vaccination on the results, the presence of antibodies in other body fluid than serum, and finally, the test in human tuberculosis.

As the object of the experimental work was to determine the clinical value of the test, the author first endeavoured to determine the reproducibility of the test. He used a variety of the antigens that have been used by other workers; these consisted of extracts of human tubercle bacilli and of BCG, as used by Middlebrook and Dubos, Lederle's OT 4 × (4 times the normal strength), alcohol-precipitated OT, dialysed OT and a preparation containing a high content of tuberculin polysaccharide.

The results show that only differences of 3 titre steps, which were 2-fold, could be regarded as significant, and as such differences are only rarely seen during an actual period of treatment, the test can be of little value for following the effects of the treatment.

When comparison was made of the titres obtained with the various antigens in sera from normal persons and from tuberculous patients, the Lederle 4 × OT gave a greater spread of titres without giving a greater number of high titres. Good reciprocal agreement was found between the extracts of human tubercle bacilli and BCG, and between the dialysed and the precipitated tuberculins, but poor agreement existed between the extracts, the polysaccharide fraction and the 4 × tuberculin.

Attempts were made to find a relationship between the titres and the state of the disease, but wide ranges of titres were observed with all the antigens. High titres were recorded in patients with limited lesions and of low activity but, in general, these patients and non-tuberculous patients showed less scatter; in these latter patients, high titres were uncommon.

Difficulty was encountered in selecting a titre which could be regarded as signifying a positive reaction; if 1 : 8 was selected the reaction was positive in 43–72% of tuberculous patients and 8–34% of non-tuberculous persons, the range depending on the antigen used, and if 1 : 32 was selected the figures became 14–28% and 0–10%, respectively. For the convenience of assessing the specificity of the reactions with the various antigens, the author regarded 1 : 16 as the limit for positivity. With this limit, the results with the various antigens for pulmonary tuberculous and control sera, respectively, were 48·8 and 12·4% with the 4 × OT, 39 and 7·6% with the precipitated OT, 44·5 and 16·9% with the polysaccharide fraction, 29·9 and 10·1% for human tubercle bacilli extract, 22·2% and nil for the BCG extract, and 41·3 and 11·9% for the dialysed OT; in no instance was there a statistical significance between the titres of sera from non-tuberculous patients and of those from the normal control persons.

When the different types of pulmonary tuberculosis were considered, significantly more positive reactions were found among the bacillus-positive patients, patients with exudative lesions, or with radiological activity, and in cases of total activity, but no difference was found between cavity and non-cavity cases. The lowest percentage of positive reactions was found

among the cases of minimal tuberculosis. However, only about one-half the cases, however extensive the disease, reacted positively. Correlation of the titres and the various antigens suggested that some antigens might be better than others but in no instance was the difference conclusive. [The reader, in attempting to follow the many analyses of the results, may have difficulty in deciding which are the better antigens, and the author himself offers no opinion.]

From follow-up investigations made on some 400 patients after periods of up to 3 years from the time of testing, the author concludes that the test is of little prognostic value and finally, as the titres observed in 31 sera from cases of sarcoidosis are similar to those in tuberculosis, he cannot justifiably draw any conclusion as to the aetiology of this disease.

Possible causes of the variability of the varying titres of the antibodies in tuberculous patients and of healthy persons are considered in the discussion, but the general conclusion of the test is that it has very limited value as a diagnostic or prognostic aid; this limited value is perhaps due to tuberculosis immunity existing on a cellular plane rather than to the presence of circulating antibodies. *S. R. M. Bushby*

LORRIMAN, G. & BENTLEY, F. J. **The Incidence of Segmental Lesions in Primary Tuberculosis in Childhood. With special reference to the Effect of Chemotherapy.** *Amer. Rev. Tuberculosis.* 1959, June, v. 79, No. 6, 756–63. [19 refs.]

There is considerable difference of opinion about the advisability of using antimicrobial drugs, especially isoniazid, in young children infected with tuberculosis. Some authors think that not only do the drugs fail to hasten the resolution but actually increase the likelihood of the development of segmental lesions, and that this counterbalances the undoubted reduction in the incidence of haematogenous complications. In this paper the authors consider the development of these lesions in 91 children admitted to hospital in Brentwood, England (29 of the original 120 had to be excluded for various reasons). Of these 50 were untreated, and 41 were treated with drugs (32 received isoniazid). The 2 groups were very fairly comparable. In each group 10 segmental lesions developed but there was a tendency for the lesions to develop earlier in the untreated group. In 8 of the treated patients the lesions developed during the use of the drugs when the regime included the use of isoniazid. 7 of the 16 children under 2 years of age treated with isoniazid developed segmental lesions compared with 2 out of 10 of the untreated, but this is not statistically significant. 12 additional children received isoniazid for 1 month only but whether these are added to either group the statistical result is not affected. The treated children were observed for an average period of 2·4 years, the untreated for 3·4 years.

It is thought that the time interval between infection and lesion development was nearer 6 than 3 months.

Symptoms associated with the onset of the lesions were slight, occasionally there was a mild fever and lassitude but usually the onset was symptomless. Illustrative case histories are given. 24% of 107 children developed segmental lesions. This rather high figure compared with other series is discussed and it is concluded that the cause lies in the type of case and admission delays.

Unfortunately as the authors point out, the numbers are rather small but it is unlikely with the fall in the tuberculosis infection rate in Great Britain that a large series will become available for study.

It is concluded that the suggestion that antimicrobial drugs induced the likelihood of segmental lesions is not proved; as in the United States Public Health Service investigation [this *Bulletin*, 1958, v. 33, 455] it was found that 80% of haematogenous complications were prevented by the drugs the authors are in favour of the use of the drugs. [This is a valuable and carefully controlled investigation with a bibliography, which should be read in full.] *F. H. Young*

CROFTON, J. **Chemotherapy of Pulmonary Tuberculosis.** *Brit. Med. J.* 1959, June 27, 1610–14, 4 figs. [13 refs.]

It is a little startling to read in the opening sentence of this account of the drug treatment of pulmonary tuberculosis from the Edinburgh School—"The right use of modern methods of chemotherapy now makes it possible to aim at 100% success in the treatment of pulmonary tuberculosis." But Crofton makes out a good case. Graphs are given showing the dramatic fall in the death-rate from pulmonary tuberculosis in Edinburgh and in the last 2 years a similar fall in the notification rate. This is understandable when he states that since 1955, of known cases out of hospital not more than 1% have a positive sputum.

He recommends that all children under 1 year with a positive tuberculin reaction should be treated with PAS and isoniazid. In those over 1 year provided that the positive reaction is the only evidence of tuberculosis he thinks that it is unnecessary, and the same applies to adolescents provided that further observation is adequate.

Where there are X-ray lesions of doubtful activity, the difficulty of ensuring that treatment is properly taken makes it advisable only to treat selected cases.

In the presence of active disease, mild cases without a positive sputum can be treated by chemotherapy and allowed to remain at work provided that it can be ensured that treatment is carried out; but those with a positive sputum and those who are unlikely to co-operate fully should at any rate start their treatment in hospital.

Great emphasis should be laid on full standard treatment to avoid drug resistance. The Medical Research Council showed that 5% of newly diagnosed patients in Great Britain have bacilli resistant to at least 1 of the standard drugs [this *Bulletin*, 1957, v. 32, 995]. The routine treatment in patients under 40 years is streptomycin 1 gm. daily, with PAS 5 gm. 3 to 4 times daily, and isoniazid 200 mgm. each day. Over 40 years of age the patient receives the streptomycin 3 times a week: this is continued whatever the result of the sensitivity tests, but in the younger group the PAS is dropped while the patient is in hospital if the bacilli are fully sensitive. On discharge from hospital 5 gm.

of PAS and 100 mgm. isoniazid are given twice daily in 1 cachet. Crofton claims that all the 239 consecutive patients with sensitive organisms treated in 1952–6, except 3 who died of intercurrent conditions, had converted by the end of the 10th month. As regards duration of treatment, of 259 patients discharged from various Edinburgh hospitals with a negative sputum, no relapses have occurred where drug treatment was continued for 15 months compared with 36% of relapses when the period was not more than 3 months.

It was found that in resected specimens only in 2 patients could bacilli be cultured when treatment had been carried out for 1 year.

Crofton considers that the main reason for resection are the unco-operative patient, and patients whose organisms have become drug resistant. He considers that in view of the evidence that only at first is there a marked improvement by the use of corticosteroids, their use should be confined to severely ill patients. In these a dramatic improvement in general well-being will keep them going until the antimicrobial drugs have an effect.

[This is a most important paper. The results claimed are in advance of any similar series; so much so that doubts may be felt as to their reliability. The abstracter has personal knowledge of the work and can vouch for its authenticity. Discussion with the author did reveal some unusually favourable local factors which may have contributed to such brilliant results.] *F. H. Young*

ORGANICK, A. B. **Toxic Psychosis due to Isoniazid. Report of Three Cases with Studies of Patterns of Isoniazid Inactivation in the Serum.** *Amer. Rev. Tuberculosis.* 1959, June, v. 79, No. 6, 799–804. [26 refs.]

Cases of toxic psychosis due to isoniazid have been reported with increased frequency now that high dosage (12 mgm. per kgm. per day) has become more common. 3 cases of toxic psychosis are reported in some detail; 1 was found to be a slow inactivator of isoniazid but the other 2 were not. In the first case there was renal insufficiency which caused intolerance to streptomycin in normal doses and confused the issue, but smaller doses of isoniazid were subsequently tolerated. In the second, who subsequently could not tolerate normal doses, there was an appreciable anaemia which may have been a factor. The third patient (aged 76) had already exhibited paranoiac symptoms but these had abated when isoniazid treatment was started; relapse started after 6 weeks' treatment with 12 mgm. per kgm. per day; removal of isoniazid led to improvement but the resumption of the isoniazid in doses of 5 mgm. per kgm. per day had a much smaller effect and treatment was able to be continued. In all 3 pyrodoxine was given and as usual it prevented peripheral neuritis but not other isoniazid effects.

It is concluded that patients treated by the large dose method of treatment should be carefully watched for psychotic symptoms. [Rather surprisingly no note is made of the fairly well-known effects of isoniazid on schizophrenics in producing relapse.] *F. H. Young*

LAUENER, H. & FAVEZ, G. **The Inhibition of Isoniazid Inactivation by means of PAS and Benzoyl-PAS in Man.** *Amer. Rev. Respiratory Dis.* 1959, July, v. 80, No. 1, Pt. 1, 26–37, 5 figs. [27 refs.]

"A method is described for the colorimetric determination of the ratio of free isoniazid to the total isonicotinic acid derivatives in body fluids in the presence of PAS.

"It has been confirmed that isoniazid inactivation is relatively constant in the individual.

"In groups of 12 to 20 patients with pulmonary tuberculosis, it was found that the addition of oral doses of either PAS or benzoyl-PAS to isoniazid therapy induces a significant increase in the concentration of free isoniazid in the plasma and urine in the majority of cases. The average of the values of all of the cases also demonstrated an increase.

"The minimal effective dose of calcium benzoyl-PAS for significantly augmenting the excretion of free isoniazid was found to be 8gm. per day. Smaller doses of benzoyl-PAS, as well as the small PAS fraction of the molecular isoniazid-PAS compound, are ineffective."

WEBB, W. R. **Pulmonary Resection for Drug-Resistant Cavitary Tuberculosis utilizing Ancillary Drugs.** *Amer. Rev. Tuberculosis.* 1959, June, v. 79, No. 6, 780–89, 5 figs. [14 refs.]

The presence of active pulmonary tuberculosis in patients whose bacilli are resistant to the 3 main drugs is a serious condition. Resection is advocated by most authorities for this state of affairs but the mortality and complication rate is high.

This paper deals with 68 resections in 62 patients with resistant bacilli, most of whom had long-standing and advanced disease. The patients were given viomycin 2 gm. twice weekly, usually with 500 mgm. of pyrazinamide (6 patients had 1 gm. of thiazosulphone) 4 times daily for 14 days before and 3 months after the operation. 5 patients died of pulmonary complications which were not directly due to tuberculosis. In 4 viomycin had to be discontinued because of toxicity and 4 had anaphylactic reactions, and sulphone produced a recurrent rash in 1 patient. 2 had radiological, 5 had bacteriological relapse, and 7 had relapses of both types; but with additional treatment 83·8% of the 62 patients were alive and well at the end of the observation period (4–56 months).

The results are definitely superior to those reported in the Veteran Administration Series (*Sixteenth Conference on Chemotherapy of Tuberculosis*, 1957, 445). A convincing case for the use of additional drugs as a cover for surgery in patients with drug-resistant organisms is made out. *F. H. Young*

YOUNG, R. C., MISENER, F. J., QUINLAN, J. J. & HILTZ, J. E. **Pulmonary Function Changes in Bilateral Resection for Pulmonary Tuberculosis.** *Amer. Rev. Tuberculosis.* 1959, Apr., v. 79, No. 4, 468–73.

After a preliminary review of the rather sparse literature on pulmonary function after resection, the

authors report their results on 29 patients after bilateral resection. A full clinical and radiological examination before and after each resection was carried out, followed by determination of minute resting ventilation, expiratory reserve volume, vital capacity, and maximal breathing capacity. The amount of lung resected varied from bilateral wedge resections to a lobectomy and 2 segments on the other side.

It is interesting to note that the pre-operative figures did not show any close relationship to the predicted results. The results showed that the reduction compared with the predicted values is surprisingly small. In the minimal disease group there was a median decrease of 16% in the actual vital capacity and an increase of 4% in actual maximal breathing capacity. In those with at least a lobectomy (12) on one side (always the upper lobe) there was a median decrease of 21% of actual values, the vital capacity was reduced by 21% of actual value, with a 17% fall of actual values in the maximal breathing capacity. The results corresponded with removal of in-between amounts of lung tissue. In some patients the post-operative results were repeated about 3 months later and a small additional improvement was found.

The authors find that the maximal breathing capacity is the most useful test. The vital capacity is reduced by the trauma to the chest wall.

[This is an interesting study well carried out. However, as the oldest patient was 49 it is not of much value when applied to the old-age group, which is the most difficult to assess.] *F. H. Young*

GLASS, R. **Forcible Detention of Patients with Active Tuberculosis.** *Pub. Health Rep.* Wash. 1959, May, v. 74, No. 5, 399–404. [13 refs.]

There are laws governing the forcible detention in hospital of recalcitrant patients with communicable pulmonary tuberculosis in many of the United States of America. These laws are, however, enforced in only a few States [this *Bulletin*, 1954, v. 29, 810].

Since 1903 New York City has had regulations for forced hospitalization. The regulations empower the commissioner of health to remove and detain tuberculous patients who present or are likely to present danger to the lives and health of other persons and have refused their voluntary co-operation. Such persons may be given a last chance by accepting voluntary hospitalization with strict adherence to hospital regulations. This is described as the "hold" procedure.

Patients in the detention service received chemotherapy or other indicated drug treatment. Transfer under "hold" is arranged to ordinary hospitals for treatment not available in detention.

Release is granted to patients whose disease becomes inactive and whose treatment and supervision can safely be continued outside. Patients are also released if they agree to co-operate: they are transferred to other hospitals under "hold".

Between July 1955 and January 1, 1958 46 men were admitted to the detention service including one readmission. 14 had moderately and 32 far advanced disease. The absence of minimal disease is noted. Their ages ranged from 21 to 72 years (average 44); 16 were alcoholics, 1 was a drug addict, 6 had criminal records, and 2 had to be removed to mental hospitals.

The known duration of the disease was 3 months to 10 years (average 44·7 months). Each of the patients had been in hospital frequently (maximum 44 times), and the time elapsed since the last attendance at a clinic or stay in hospital ranged from 2 days to 2 years (average 3½ months). 22 patients had broken their promise to stay in hospital voluntarily under "hold".

The disease became inactive in 20 during detention or under hold, 4 men absconded from non-detention hospitals, 3 with inactive disease did not attend for supervision, 1 died in detention from a pulmonary haemorrhage and 2 in other hospitals, one of them from a non-tuberculous condition. At the end of the period 18 were still in detention of whom 7 showed improvement.

The patients detained represent a small proportion of those in New York with active pulmonary tuberculosis who merit detention, and stimulated by the above results the authorities contemplate an expansion of the detention programme. [The statute authorizing the forcible detention of recalcitrant tuberculous patients in Northern Ireland was repealed this year.]

H. G. Calwell

TODOROVITCH, K. Rechutes, récidives et manifestations de "l'encéphalite larvée"—signes de Voujitch-Ristitch—au cours et à la fin du traitement de la méningite tuberculeuse. [**Relapse, Recurrence and the Manifestations of "Larval" Encephalitis in Tuberculous Meningitis**] *Bull. Acad. Nat. Méd.* 1959, v. 143, Nos. 19/20, 429–33.

In 1950 Todorovitch and his colleagues analysed the clinical course of 390 patients with tuberculous meningitis who had been treated with streptomycin in the 2 previous years [this *Bulletin*, 1951, v. 26, 760]. They drew attention to the occurrence of relapse in 8% and of recurrence in 8·6% and showed that these were generally the consequence of too small dosage and too short duration of treatment.

Nevertheless there were other factors favouring relapse such as extension of the disease process, meningeal lesions themselves, circulatory changes, as well as the toxic action of the drug on the auditory and optic nerves, which caused treatment to be interrupted. The prognosis appeared to be more favourable when relapse occurred late and was of short duration.

Recurrence of the disease was seen after intervals of several months or even years and most often after the disappearance of all the classical signs of meningitis. They were usually preceded by a worsening of the general state and changes in the cerebrospinal fluid before the development of the meningeal syndrome.

During the period 1947–58 the author treated 2,000 patients with tuberculous meningitis in Belgrade, at first with streptomycin alone, later with other antituberculous drugs and in the last 2 years of the period steroids were added to the armamentarium. His experience showed that a recovery rate of 80–90% may be attained if the condition is diagnosed in time and adequate treatment applied. The prognosis in relapse

and recurrence is better than when streptomycin alone was used.

It is generally admitted that the term tuberculous meningitis ordinarily used to describe tuberculous disease of the meninges does not correspond, exactly to the anatomical distribution of the lesions which extend more or less deeply into the neighbouring cerebral tissue. The diagnosis of the presence of these deep lesions is not particularly difficult in the presence of corresponding clinical signs but these may be very difficult to detect.

"Larval encephalitis" is accompanied by the following neurological signs:

Deviation of the wrists when the arms are extended horizontally forwards; narrowing of the palpebral fissure; elevation of the eyebrow on one side when the gaze is fixed on a moving finger held at the side or a little below eye level; absence of swinging movement of an arm during walking with restoration of movement when the other hand is given an object to hold; hands held with the palms facing backwards while walking; staggering gait while walking with the eyes closed and the persistence of bilateral nystagmus in patients with no lesion of the internal ear.

The signs of extrapyramidal disease mentioned above are evidence of the cerebral grey matter being affected in the course of tuberculous meningitis.

H. G. Calwell

GROTH-PETERSEN, E. **The Risk of Tuberculosis as a Guiding Factor for Tuberculosis Eradication.** *Acta Tuberculosea Scandinavica.* 1959, Suppl. 47, 132–8, 1 fig.

If tuberculosis is to be controlled effectively it is necessary to define the groups of the healthy population in which new cases are likely to arise and to employ intensive casefinding and preventive measures in those groups.

In 1957, 1,105 new cases of pulmonary tuberculosis and 154 relapses of patients previously considered cured were reported in Denmark. The smallest number occurred in the 5–15-years age group in both sexes. The highest peak in females was between 25 and 30 years, and in males there were peaks at 20–25, 30–35 and after 50.

As schoolchildren and young people are the most frequently examined the low incidence in the 5–19-years group is a reality but as older people are examined least the reported incidence of the disease in those over 25 years must be considered an understatement.

The tuberculosis clinics examine one-fourth of the adult population each year but to a large extent the same individuals are examined year after year.

The need to keep young spontaneous tuberculin reactors under supervision is indicated by the fact that among healthy spontaneous reactors aged 15–24 years 3 to 4 times more new cases of tuberculosis arose in a stated period than among spontaneous reactors over 45 years and 8 times more than those of their group who had been vaccinated with BCG.

It is emphasized that among young persons already infected the risk of developing tuberculosis increases with the degree of tuberculin sensitivity. Among those with induration of more than 18 mm. (Mantoux 10 TU of PPD) the yearly rate was about 120 per 100,000 compared with about 30 in those with induration of less than 12 mm.

Much more important for prognosis is the presence of a suspicious radiological abnormality (other than definite calcification), signs of active tuberculosis being absent. The annual case rate in this small group was 3,000 per 100,000 during the first 3–4 years of observation, i.e. about 12%. This group must therefore be checked frequently regardless of age and thought should be given to the prevention of the evolution of disease by chemotherapy.

About one-half of the total population of Denmark [4½ million, approx.] is spontaneous'ly tuberculin positive and Groth-Petersen estimates that 85–90% of new cases of tuberculosis will arise in that group and be responsible for the majority of new infections in non-reactors and BCG-vaccinated persons. Non-reactors refusing BCG should be tested periodically.

For the vaccinated part of the population it appears that the longer the interval after vaccination the greater the risk of tuberculosis; for them also high tuberculin sensitivity and abnormal radiological findings are bad omens.

In 1957 some 841,000 adults were examined in chest clinics in Denmark and 894 new cases of tuberculosis discovered. About 65% of the new patients were found among the 12% who were examined because of symptoms or contact. The incidence in this small group was 17 times higher than in the large routine group. The low rate in the routine group suggests the question whether a more worthwhile result could not be obtained partly by seeking out persons not previously examined and partly by a more selective plan such as getting more people over 45 examined, in whom just a single examination is especially valuable.

H. G. Calwell

SPIESS, H. Chemoprophylaxe und präventive Chemotherapie gegen die Tuberkulose. [**Chemoprophylaxis and Preventive Chemotherapy of Tuberculosis**] *Deut. med. Woch.* 1959, Aug. 7, v. 84, No. 32, 1410–5, 1435–6. [Numerous refs.]

The author distinguishes between chemoprophylaxis and preventive chemotherapy. The first denotes the administration of a specific drug to an uninfected person in order to prevent the establishment of infection; the second indicates treatment of a person known to have been infected, in order to prevent the development of disease by generalization.

The drug generally used for chemoprophylaxis is isoniazid. Its value has been demonstrated by many animal experiments, details of some of which are given.

Experience of isoniazid prophylaxis in human beings is confined to isolated observers. The trials have not been controlled statistically and the results are suggestive rather than conclusive. A trial is going on in the United States in which 3,886 persons aged 2 months to 70 years are taking part. They come from 1,198 households in which a case of tuberculosis has recently been discovered and include both reactors

and non-reactors. One half receives isoniazid and the other half inert tablets. Adults are given 3–7 mgm./kgm. of isoniazid daily and children 5–10 mgm. for 1 year. Any person requiring treatment for tuberculosis is excluded and treated. The results will be reported in due course.

There is experimental evidence also of the value of preventive chemotherapy but there is not a great deal of information about its use in man. A trial is going on in France on children who have undergone tuberculin conversion within 6 months. Experience there and elsewhere suggests that generalization of the disease is less frequent in treated than in untreated children. There is also published evidence that the complications of primary infection such as meningitis are reduced by preventive chemotherapy.

A trial made in the United States showed that in a group of 2,750 infected children of whom one-half were given isoniazid (4–6 mgm./kgm.) and the other half inert tablets daily for 1 year, 5 of the treated and 26 of the untreated children developed complications. Isoniazid gave 80% protection. It remains to be seen whether complications will develop after the conclusion of the preventive treatment; it is considered unlikely that meningitis will do so as it usually occurs in the first 12 months after infection.

The following indications for chemoprophylaxis with isoniazid are given: (a) healthy uninfected persons who are temporarily exposed to special risk of infection; (b) uninfected healthy infants and young children who may have been exposed to infection.

Preventive chemotherapy is recommended for the following: (a) Persons of any age whose infection is known to have occurred within the previous 6 months, all infected infants below the age of 3 years and children at puberty who show signs of reactivation of an old focus of tuberculosis; (b) tuberculous persons showing exacerbation of disease or in danger of reactivation because of intercurrent infection such as measles, whooping cough or influenza.

Chemoprophylaxis is not a substitute for BCG vaccination. They may be combined in suitable cases. The most important method of preventing tuberculosis is the discovery, isolation and treatment of infectors. The tuberculin test is a better means of discovering newly infected children than X-ray examination (provided of course that they have not been vaccinated with BCG). *H. G. Calwell*

EBINA, T. & SAITO, T. **The Protecive Value of Non-lyophilized and Lyophilized BCG Vaccine against Tuberculosis.** *Acta Tuberculosea Scandinavica.* 1959, v. 37, Nos. 1/2, 162–74.

The protective value of BCG vaccination was assessed by comparing the morbidity and mortality from tuberculosis in 3,211 vaccinated and 2,615 unvaccinated students and schoolchildren in Japan. All were non-reactors to tuberculin (erythema and oedema of less than 10 mm. to Mantoux test with 0·1 mgm. of OT). Fresh vaccine was used, the dose being 0·03 mgm. of bacilli.

The period of observation was 1–4 years, and the diagnosis of tuberculosis was made by X-ray examination of the chest. Fatal tuberculosis occurred in 13 (0·48%) of the unvaccinated and in none of the vaccinated.

The morbidity rate in each sub-group except one was definitely lower in the vaccinated persons than in the unvaccinated. It was seen that the greatest difference occurred in student nurses who were observed for 4 years and in whom the rates were 14·4 per 1,000 in 208 vaccinated and 202·0 per 1,000 in 198 unvaccinated. This difference was highly significant.

The types of pulmonary lesions seen were:

	Number	Primary lesion		Post-primary lesion		Pleurisy	
		No.	%	No.	%	No.	%
Unvaccinated	2,615	26	0·97	20	0·76	23	0·87
Vaccinated	3,211	23	0·69	2	0·06	5	0·14

It was thus seen that although primary tuberculosis occurred with about the same frequency in the vaccinated and unvaccinated, post-primary and chronic tuberculosis as well as pleurisy occurred less frequently in the vaccinated than in the unvaccinated. The differences were significant.

Morbidity from tuberculosis, the type and course of the disease were further compared in vaccinated and unvaccinated persons aged 14–25 years who, because of symptoms suggestive of tuberculosis, attended the authors' out-patient clinic or were treated in hospital during the years 1949, 1951 and 1953.

Patients attending in 1949 had received only fresh vaccine, those in 1951–53 had received either fresh or lyophilized vaccine. Of those observed in 1953 it was known that 54·4% had received fresh and 45·6% lyophilized vaccine.

Tuberculosis was observed about twice as often in unvaccinated as in vaccinated persons. The rates in 2,147 vaccinated and 1,990 unvaccinated persons were 30·6 and 65·5% respectively. Details of the types of disease seen and of their classification are given.

The ratio of primary lesions in both groups was about the same for each year of observation. It was significantly lower in the vaccinated than in the unvaccinated. Moderate or far advanced tuberculosis was found more often in the unvaccinated and minimal tuberculosis more often in the vaccinated.

Among the out-patients acute forms such as miliary, pneumonic and mixed type with cavitation occurred oftener among the unvaccinated while undurative types occurred oftener among the vaccinated. Neither miliary nor pneumonic tuberculosis occurred in the vaccinated.

The course of the disease was more favourable in the vaccinated and the mortality rate was lower. No significant difference was seen in the occurrence of tuberculosis and the type of disease among 252 persons who had received fresh vaccine and 378 who had received lyophilized vaccine. *H. G. Calwell*

VENEREAL DISEASES

DEL VECCHIO, G. Aggiornamento statistico, epidemiologico ed organizzativo sulla lotta contro le malattie veneree in Italia per gli anni 1955–56. **[The Anti-Venereal Disease Campaign in Italy in 1955–56]** *Ann. d. San. Pubblica.* Rome. 1959, Mar.–Apr., v. 20, No. 2, 239–84. English summary (3 lines).

The author of this report which deals with statistics, epidemiology, and organization, is the Medical Inspector-General of the Italian Ministry of Health; the paper is therefore authoritative.

The progress of the campaign is described under various headings, and the biennium is compared with 1954 and even with 1937; since the paper consists very largely of figures it is not easily summarized.

In general, compared with 1954 there was a considerable increase in 1955 in syphilis (all forms), and a further increase in 1956; gonorrhoea figures showed a slight reduction, those for soft chancre remained practically unchanged, and there was a considerable reduction in lymphogranuloma venereum.

Syphilis. The numbers of notifications are practically the same for 1955–56 as for 1937, but there has been a very marked reduction in the primary and secondary forms which now make up rather less than 10%, as against 60% in 1937. There was an increase in other forms, particularly congenital (including sero-positive and sero-negative forms and cases "under observation"), in 1955 and a further increase in 1956. However, compared with 1937 the number of notifying centres has quadrupled.

There are many very interesting tables, showing among other things the administrative regions where there has been an increase. These are not always the same in the 2 years but Sicily had high figures for both years and also Campania [where the effect of conditions in Naples must be important], but Rome on the contrary does not figure in the list, and its administrative region does not show an increase.

Gonorrhoea. Compared with 1954 there was a slight reduction, but the figures are subject to the qualification that non-gonococcal urethritis, and vulvo-vaginitis, are now being considered separately whereas before they were included. The author emphasizes that, notwithstanding the use of antibiotics, in 1955 chronic cases constituted 33% of the total, and in 1956 28%.

Maternity and Child Welfare Service. Discussing the usefulness of the anti-venereal section of this service, Del Vecchio points out that the number of women diagnosed as syphilitic is high. In 1955 the primary-secondary forms were nearly 5 times as high as those for 1954, the increase being almost exclusively in Campania; the position improved considerably in 1956. The predominant forms are the clinically latent and the sero-negative congenital forms.

Social Insurance. As regards the Health Insurance Societies, notification is not compulsory and was only started in part in 1955. Even so, the figures for the biennium form over 20% of the national total. Syphilis was the main disease and males were more affected. Campania again occupied first place in numbers. Late syphilis formed over 55% of all VD cases assisted, and gonorrhoea formed 15% of the 1955, and over 19% of the 1956 national figures.

Prostitution. There is an extensive discussion on the question of licensed houses and the position of the "free" prostitute whether with, or without, a health department permit. The figures of those examined are very high, nearly 69,000 in 1955 and about 56,000 in 1956. In both years over 30% had some disease, most of which was venereal. Syphilis was the most frequent form, the infectious types being most common in those outside the licensed houses, without a permit. Among "occasional" prostitutes gonorrhoea was most frequent in 1955 but syphilis in 1956. The gonorrhoea was acute in 75%.

The reduction in the number of prostitutes in licensed houses found with diseases was considerable, but the reduction in the numbers with detected disease among the peripatetics is considered alarming as it is apparently due to a relaxation of sanitary vigilance in certain areas.

Laboratory tests. In addition to the WR the TPI test was used in the university clinics.

Health Visitors. The section on their work is one of the most important in the whole review. The value of such visitors not only in tracing contacts, but in dealing with untreated cases particularly in mothers and children, and in dealing with defaulters, is particularly stressed. The figures given are really surprising and reflect the greatest credit on the Health Visitors who, as Del Vecchio points out, are the qualified persons who can carry out social and sanitary duties not only in the family but in general.

Health Insurance Societies. There is criticism of these societies for their lack of co-operation in not employing Health Visitors in the domiciliary service with the unmistakeable possibility that sanitary activities may have to be imposed on such societies.

In conclusion the author makes two negative points as follows:—

1. The infectious forms of syphilis increase where proper vigilance is not exercised on prostitutes outside the licensed houses.

2. The absence of any anti-venereal-disease social service in the Health Insurance Societies.

[As the licensed houses have now been closed, it will be interesting to see how the anti-venereal-disease campaign progresses. The author's justifiable enthusiasm for the work of the Health Visitor could be communicated with advantage to the producers of the Younghusband report.] *W. K. Dunscombe*

IBARRA, L. M. **The VD Control Program of the Manila Health Department.** *J. Philippine Med. Ass.* 1959, Apr., v. 35, No. 4, 219–23.

This programme consists of (1) contact tracing, (2) screening including compulsory examination of certain workers such as waitresses and government employees, (3) voluntary blood testing and (4) education of the public.

Of 635 contacts reported 463 were visited and 196 (42%) found to have gonorrhoea and 1 syphilis; of male patients with venereal disease 50% were infected

by prostitutes, 36% by waitresses, 13% by hostesses and 4% by others [these figures seem to add up to 103].

Of those workers subjected to compulsory examination 9·3% of those giving positive serum tests for syphilis were found to be suffering from latent syphilis [what the diagnosis was in the other 90·7% is not stated]. Among those voluntarily tested (6,942) 200 gave positive reactions; in 70 of these 6 had latent syphilis. Education of the public was on the usual lines.

Diagnostic and treatment facilities were adequate though cultures for gonorrhoea were only carried out in special cases. The treatment of gonorrhoea was 600,000 units of PAM, repeated if complications were present; of early syphilis 4·8 mega units, of latent syphilis 6–9 mega units, of late syphilis 6–12 mega units, of congenital syphilis 1·5–6 mega units and of pregnant syphilitic women 6 mega units, all of PAM. For chancroid and lymphogranuloma venereum sulphonamides are tried first and if these fail broad spectrum antibiotics. Other activities include post-treatment observation; a training centre exists for instruction in venereal diseases for physicians, nurses, interns and technicians; some research work is also being carried out. Venereal diseases are compulsorily notifiable by law but only 2–3% of private practitioners comply.

[The VD service in Manila certainly seems efficient but it would be interesting to know what success in reducing VD has been achieved.] *T. E. Osmond*

Migne, J., Bénazet, F. & Reboul, E. Étude critique des réactions dites "quantitatives" utilisant les antigènes cardiolipidiques. [**A Critical Study of Quantitative Reactions employing Cardiolipin Antigens**] *Rev. d'Hyg. et de Méd. Sociale.* Paris. 1959, Mar., v. 7, No. 2, 148–61, 7 figs.

These reactions are useful for (1) disclosing biologically false positive reactions, (2) indicating the stage of infection, and (3) controlling treatment.

239 sick persons were studied including 159 syphilitics (11 primary, 26 secondary, 13 tertiary, 6 nervous, 11 congenital and 92 sero-positives); other diseases included malaria, infective mononucleosis, infective hepatitis and virus pneumonia, The significance of rising and falling titres, low titres, discordant results with 2 or more reactions, is pointed out. The reactions employed were Kolmer and Debains complement fixation and Kahn and Kline flocculation and the results to be expected in untreated and treated syphilis in various stages, in other diseases liable to cause false positive reactions and in relapses and reinfections are set out in the text and in 7 figures and 1 table; several case reports are included.

[There is nothing new in this article; many others have been carrying out routine quantitative tests over many years.] *T. E. Osmond*

Bekker, J. H. & Onvlee, P. C. **The Reiter Protein Complement Fixation Test in Experimental Syphilis.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1959, v. 25, No. 1, 38–40.

These authors evaluated the value of the RPCF test (Reiter protein complement-fixation test performed with the protein fraction of the Reiter spirochaete) on infected rabbits in parallel with the TPI test and the Kolmer test with cardiolipin antigen.

In the first series of 5 rabbits the Kolmer test became positive after 7–8 days followed shortly by the RPCF and TPI tests; in a second series of 5 rabbits treated with penicillin within 3 weeks after the development of orchitis the Kolmer became negative after 4–6 weeks, the TPI after 6–10 weeks and the RPCF after 10–20 weeks; in a third series of 5 rabbits treatment was delayed for 3 months after the orchitis had developed; in 2 rabbits all tests were positive after 40 weeks, while in the other 3 the Kolmer alone became negative after 4 weeks while the other 2 were still positive after 45 weeks.

Thus the RPCF appears equal to the TPI; the longer the duration of infection the longer the former remains positive; it seems that the value of the RPCF test is in diagnosis rather than in test of cure.

T. E. Osmond

Rajam, R. V. & Sowmini, C. N. **Oral Tetracycline in the Prevention of Prenatal Syphilis.** *J. Indian Med. Ass.* 1959, June 1, v. 32, No. 11, 435–7.

It is generally agreed that penicillin given in time will prevent prenatal syphilis in the large majority of cases; however, when the patient is sensitive to penicillin another remedy must be found.

These authors treated 12 pregnant syphilitic women with Achromycin [tetracycline] 500 mgm. orally every 6 hours to a total of 24 gm.; 10 healthy children were born, 1 mother was lost to observation and 1 child died owing to difficult delivery (but was considered to be non-syphilitic).

There were no adverse side effects of the drug.

T. E. Osmond

Vor Dem Esche, P. Erfahrungen bei serologischen Luesuntersuchungen von Blutspendern [**Experience in the Serological Examinations of Blood Donors for Syphilis**] *Arch. f. Hyg. u. Bakt.* 1959, Aug., v. 143, No. 5, 348–56. [Numerous refs.]

An account is given here of the results of the testing of over 34,000 sera from blood donors by the cardiolipin micro-flocculation test (CMT) and the findings are then discussed in relation to the incidence of unrecognized syphilitic infection. Some of the published work on the specificity of this test is quoted and the author describes the modifications of the original method which were introduced by him in simplification of the technique.

Among the total of 34,422 sera tested there were 62 which gave a positive or doubtful reaction. These 62 sera were then further examined by complete serological investigation by 4 other tests, when 13 gave a negative reaction with all tests. Fresh samples of sera in those instances (49) where a positive had been obtained in 1 or more of the additional tests were then re-examined. Ultimately the opinion was reached that the number of positive sera in the total of over 34,000 was 31, *i.e.* 0·09%. In 25 of these, syphilitic infection of the persons concerned had not previously

been recognized. A table gives the age distribution of these 25 positives—in the 18–30-year group of blood donors the rate was 2 per 10,000 and in the 30–60-year group the rate was 20 per 10,000. In the detailed discussion it is stated that this age distribution reflects the widespread syphilitic infection which occurred in the war and post-war years. *M. E. Delafield*

BROWN, W. J. & SUNKES, E. J. **A Recent Study of the Results of Premarital Serologic Testing in a Southern State.** *Southern Med. J.* 1959, June, v. 52, No. 6, 707–10.

After calling attention to the incidence of syphilis in U.S.A. in 1940 and since, and noting that, by 1957, 42 States had premarital testing laws these authors point out that in recent years early syphilis, so far from decreasing, has actually been increasing.

They report a study of 25,586 premarital bloods tested in Georgia, of which 814 (3·1%) showed reactivity; 136 of these subjects were brought to treatment, 119 returned to treatment, 357 had previously been adequately treated, 52 were not infected and 6 had been given "epidemiologic treatment"; 144 were of unknown dispositions. The large majority of those in the first 2 treated groups (255) were in the early or late latent stages but 3 primary and 10 secondary cases were found.

It is concluded that a case has been made out for continued premarital blood testing and it is recommended that a study be made of the law and blood testing be carried out by the State Health Department. *T. E. Osmond*

WELLS, B. T., KIERLAND, R. R. & JACKMAN, R. J. **Rectal Chancre. Report of a Case.** *Arch. Dermat.* 1959, June, v. 79, No. 6, 719–21. [12 refs.]

Primary syphilis of the ano-rectal region is probably not so rare as might be expected from the few cases reported in the literature, particularly if is true, as reported, that in the U.S.A. 37% of all males indulge in pederasty at some time in their lives.

These authors report a case of a male, who, incidentally, denied abnormal sexual practices, who had an indurated ulcer 2 cm. × 2 cm. on the anterior rectal wall 7 cm. above the dentate margin. Dark ground examination was positive as were a battery of serum tests for syphilis (several of them repeated after 3 days). 600,000 units of penicillin daily for 10 days brought about healing of the ulcer and serum tests became negative or weakly reactive (presumably a few months later, but the patient was seen "in the summer of 1958" and a follow up examination was carried out in "early January, 1958"). *T. E. Osmond*

FIUMARA, N. J., TODD, B. P., YOUNG, Hazel D. & WILSON, Janet G. **An Outbreak of Gonorrhea in Massachusetts—1957.** *Amer. J. Pub. Health.* 1959, July, v. 49, No. 7, 924–36. [10 refs.]

This report concerns 26 persons involved in an outbreak of gonorrhoea started by a single individual in a town of 23,000 people; most of the patients came from a low socio-economic group and from broken homes and lacked moral or religious convictions; most were drinkers. In Table I are named 9 persons each of whom named 2–10 contacts; all those found infected were treated and interviewed for contacts; full details are set out in Table II. Details are also given in the text of each patient's age, features, manners etc.; these do not seem very helpful since some of the females were attractive, others not; males were seldom in steady work. All were white except 1, the average age was about 27, 40% were single, 40% separated or divorced and 20% married.

The lesson to be learned is that in most communities there is a reservoir of disease and when this is discovered contact tracing is of great importance; the authors think that sexual intercourse is often motivated in the female by "sexual aggression" [but is it not merely instinct?]. Rehabilitation in these cases is difficult and often impossible, with the result that gonorrhoea can be controlled but never eliminated.

The general picture is that of life in the lower stratum of any town population particularly where promiscuous females congregate. *T. E. Osmond*

STUART, R. D. & CROOKES, Eileen M. L. **Laboratory Policy in the Diagnosis of Female Gonorrhoea Culture or Smear.** *Pub. Health Lab.* 1959, Mar., v. 17, No. 2, 41–5.

These authors found that cultures were twice as successful as smears in diagnosing gonorrhoea in women. Coliform bacilli proved a bugbear in the former and to overcome this Aerosporin (Polymyxin B sulphate) was added to the culture medium to a final concentration of 1 microgramme (10 units) per ml.

Specimens were received from 3 clinics (A, B and C); repeat specimens were rarely possible in clinic A but were so in B and C. It was decided therefore, in view of the great success of cultures, to abandon smears from B and C but to retain them from clinic A. The very successful results of cultures rendered this possible and saved many hours of technician time without lowering efficiency.

The "transport" medium consisted of agar (Bacto) 6 gm., $CaCl_2$ (1%) 20 ml., thioglycollic acid 2 ml., Na glycerophosphate (20%) 100 ml., methylene blue (0·1%) 4 ml. and aq. dist. (Cl-free) 1,900 ml.; *p*H 7·4 with NaOH. The culture medium was a modification of Peizer's with a yeast extract; the addition of Aerosporin reduced failures in 1957 from 1·5% to 0·7% from clinic A and from 1·5% to 0·5% from clinic B.

Detailed results are set out in 2 tables. *T. E. Osmond*

LANDMAN, Gerda S. & GELMI, O. **Asymptomatic Gonorrhea in the Male.** *Southern Med. J.* 1959, June, v. 52, No. 6, 750–52, 1 fig.

172 asymptomatic male patients suffering from gonorrhoea were investigated at the District of Columbia General Hospital [see also this *Bulletin*, 1958, v. 33, 1128]; these had little or no "subjective discomfort". 16 were under 20, 91 between 20 and 30, 41 between 30 and 40 and 24 over 40; the incidence was 21·3% of all male patients.

Treatment consisted of 1·2 mega units of penicillin; the cure rate is not given; various reasons are given for the absence of symptoms, self medication being one.

In a figure are given details of an infected asymptomatic teenage boy, investigation of whom resulted in the treatment of 6 additional patients.

[It is not easy to follow this paper because "symptoms" and "signs" appear to be used interchangeably; as the large majority of the patients were Negroes it is not surprising that symptoms were absent or negligible in so many cases.] *T. E. Osmond*

THURMAN, J. R. **Evaluation of Treatment of Acute Gonorrhea in the Male with Varying Dosage Schedules of Penicillin V Potassium.** *Antibiotic Med.* New York. 1959, May, v. 6, No. 5, 295–6.

An assay was made of the effectiveness of a single oral dose of penicillin V potassium; 18 male patients were given 750 mgm. of the antibiotic while a control group of 22 were given 500 mgm. followed by 250 mgm. every 6 hours to a total of 1,500 mgm.

Of the first group 66·6% were clinically well within 48 hours, 22·4% were improved and 11% showed no improvement in 48 hours; the corresponding figures for the control group were 77·3, 13·7 and 9.

The advantage of the single dose is that it is certain that the patient receives it; the cure rate does not appear high but the numbers are too small for any definite conclusions to be drawn. *T. E. Osmond*

OTHER COMMUNICABLE DISEASES

The order of papers in this section is as follows:— Tetanus; other diseases.

COLANGELO, C. **Compression Fractures of the Thoracic Vertebrae in a Patient with Tetanus.** *J. Amer. Med. Ass.* 1959, May 23, v. 170, No. 4, 455–7, 2 figs.

The case described here, a boy of 16, must surely be of very rare type, or, at least, of a type very rarely recognized. It was an "idiopathic" case, no wound being found as a possible source, and it was presumed that the toxin was absorbed from the mouth or pharynx, since foetid gingivitis with pharyngitis and ulcers of the tongue were present when the patient was admitted to hospital with symptoms of tetanus. The most rare feature, however, was the compression fractures of the bodies of the 3rd to the 9th thoracic vertebrae found in the X-ray film taken on the 19th day of illness; but this film would have been difficult to evaluate, had not an earlier lateral chest film been available for comparison. [In fact the fractures are not apparent in the illustration, although the bodies of the vertebrae seem to be compressed.]

During the course of the disease, painful tetanic spasms of the neck and back, opisthotonos, trismus, and frequent troublesome cough occurred daily for some 2 weeks; and during the coughing there were 3 episodes of severe dyspnoea, and cyanosis for some 10 minutes, and even syncope in one of these episodes. The peak of the symptoms occurred about the 19th day, although occasional tetanic spasms and opisthotonos were still present at the end of the 4th week. By the 7th week, recovery was complete.

A combination of drugs was used in treatment, including chlorpromazine 100 mgm. daily for the first 2 weeks, 150 mgm. daily in the 3rd week, 200 mgm. daily for the next 3 weeks and 100 mgm. daily for a final week. [The spasms did not appear to be very effectually controlled; the dosage of chlorpromazine may have been too small in the critical earlier period.] *H. Stanley Banks*

ECKMANN, L. Tetanusprophylaxe bei Verletzten und Therapie des Starrkrampfes. [**Tetanus Prophylaxis and Treatment**] *Ztschr. f. Präventivmed.* Zurich. 1959, June, v. 4, No. 6, 210–18, 1 chart.

It is not generally realized that tetanus has a considerable prevalence in Switzerland and the neighbouring countries. In 1952 a total of about 3,500 deaths from tetanus were registered in these countries, but as the disease is not notifiable the actual number of infections cannot be determined. The author of this paper discusses the imperfections of immunization by serum injection by reference to the literature and particularly the experience of this procedure in the British army in World War I. The extreme difficulties of the treatment of severe tetanus are described. The value of active immunization by toxoid is discussed but as this procedure is not as yet carried out systematically the problem of prophylaxis becomes urgent in cases of wounds in which there is danger of tetanus infection. In such instances it is likely to be necessary to give serum injections but these should then be combined with active immunization. *M. E. Delafield*

VERVOORN, J. D. **Active Tetanus Immunization in Ashanti-Ghana.** *Trop. & Geograph. Med.* Amsterdam. 1958, Sept., v. 10, No. 3, 277–80.

The district served by the author's hospital, in Ashanti, like the whole of Ghana has a high incidence of tetanus. Mortality, even with early and efficient treatment, is very high. An attempt was made to interest the population in active immunization, but out of 9,000 given first doses only 300 returned for a second dose. It was then decided to give 0·5 ml. tetanus toxoid to all out-patients as a routine, repeating the dose after a month. "No doubt some patients were given as much as three to four times 0·5 ml. in this way." Tetanus admissions to the hospital in the following 9 months declined to one-fifth of those in the corresponding period of the previous year.

[As an isolated effort, this scheme certainly prevented a number of people from getting tetanus and can have had no harmful consequences. It would be inadvisable for *every* hospital in a country such as Ghana to give tetanus toxoid indiscriminately, on account of the high proportion of out-patients who visit more than one. The author deserves credit for pioneering

a valuable procedure which the organized field medical services could expand logically.] *B. B. Waddy*

CH'IU, Fu-Hsi, HOU, Tsung-Ch'ang, HUANG, Ping-Shan, LIU, Wei-Ch'ang, SUNG Hsi-Yü & LI, Ying. **Epidemic Hemorrhagic Fever. Investigations in T'uliho Area, Inner Mongolia, and Clinical Study of 104 Cases.** *Chinese Med. J.* Peking. 1959, June, v. 78, No. 6, 515–31, 2 figs. [18 refs.]

[This article, while offering little that is new, provides a useful recapitulation of the features of this important disease.]

The disease is thought to be due to infection with a virus, as yet unidentified, and may well be a zoonosis; the essential lesion is a widespread capillaritis leading to wide dilatation and increased permeability of the capillary wall. The geographical distribution is limited to the Eurasian land mass, and its presence has been recognized from Czechoslovakia, throughout the Southern states of the Soviet Union, across Siberia and China to Korea. The disease varies somewhat in its general features from East to West, for in Siberia and beyond, renal damage is a prominent feature while in the European form the kidneys usually escape damage.

This paper records experience gained in an epidemic which occurred in 1955 in the T'uliho District of Inner Mongolia, where epidemiological evidence suggested the presence of a reservoir in wild rodents, mites being the probable vectors. In all, 80 typical and 24 atypical examples of the disease were studied. The epidemic lasted from mid-September until late November, with the highest incidence during the 4 weeks from mid-October. The highest attack-rate was in adult males and probably reflected their greater risk of exposure to the vector during agricultural operations.

The disease often manifested 5 phases, febrile, hypotensive, oliguric, diuretic and convalescent. These often lacked clear demarcation and milder examples of the disease might lack hypotensive, oliguric and diuretic episodes. After an incubation period estimated at 2–3 weeks, the illness began acutely with severe malaise, fever, rigors, headache, anorexia, vomiting and constipation. The average duration of the febrile phase was 4·7 days (range 3–13 days) and its range 38–40°C. the highest recorded temperature being 41·5°C. (106·7°F.). The pulse rate was increased proportionately with the temperature. At this stage the skin capillaries were widely dilated, the body flushed and the face suffused, while a peculiar type of dermatographism lacking a weal was often shown. Haemorrhagic manifestations included petechiae beneath the skin, conjunctival and buccal mucosa; purpura might develop and epistaxis, haematuria and haemorrhage from the bowel might be troublesome. Consciousness might be clouded and signs of meningeal irritation were noted in occasional patients, in some of whom the cerebrospinal fluid contained red blood cells. Jaundice was never seen and the spleen never became palpable though slight swelling of the lymph nodes was occasionally found.

Investigation showed little or no anaemia but usually a moderate polymorphonuclear leucocytosis; a constant finding, however, was a diminution in the platelet count to between 80,000–190,000 per cmm. The bleeding time was prolonged in a few patients but the coagulation and prothrombin times were normal. Albuminuria, with the presence of red cells, leucocytes and casts began on the 2nd to 5th day of the disease.

The hypotensive phase usually began on the 4th day and might culminate in dangerous or even fatal shock. It was due to two factors, capillary dilatation and depletion of the circulating volume by diapedesis of plasma and cells through the damaged capillary wall. The hematocrit was raised, the highest reading being 66%.

Oliguria then developed and might progress to complete anuria. The blood urea concentration rose rapidly and the alkali reserve fell, but as the uraemic state progressed hypertension supervened and often led to further haemorrhagic manifestations.

The diuretic phase, which usually heralded recovery began about the 12th day and persisted on the average for 9·9 days: in a few instances this led to "secondary shock" owing to derangement of electrolytic balance. Convalescence was protracted and complete health might not be regained for 2 months.

The case mortality among the 80 typical examples of the disease was 11·3%, death being due to shock or to uraemia with acidosis. The outstanding changes at autopsy comprised haemorrhagic necrosis of the pituitary and suprarenal glands, sub-epicardial and sub-endocardial haemorrhages and extravastations of blood beneath the meninges and periosteum and under the lining membrane of the hollow viscera.

In the management of such patients it was considered wise to disinfect their bodies and clothing and to disinfect all dejecta. No specific therapy was discovered since sulphonamides, penicillin, streptomycin, chloramphenicol and the tetracyclines all proved ineffective. The outcome therefore was largely determined by careful nursing and the efficient management of pyrexia, shock and uraemia.

The investigating team carried out some research on the mechanism of coagulation in 7 patients, among whom they demonstrated increases in the blood heparin level in 5, and an increase in both heparin and antithrombin in 1, "The fibrinogen B test was positive in 4 of the 7 cases."

3 full case histories are given.

[Those interested in this disease will find that this article provides an exhaustive account of its clinical manifestations.] *J. H. Walters*

BARRERA, B. **Cat Scratch Disease.** *J. Philippine Med. Ass.* 1959, Apr., v. 35, No. 4, 236–8.

This short paper on a case of cat scratch disease was read before a meeting of the Section of Medicine of the Philippine Medical Association in 1953. At that time it was the first case of cat scratch fever seen and recorded in the Philippines. It occurred in a boy aged 11 years who developed a non-suppurating inguinal adenitis about 40 days after being scratched by a kitten in the thigh. Intermittent fever was present for about a week. Adenopathy persisted for about 3 weeks. The intradermal diagnostic test was positive. Some of the clinical, diagnostic and histopathological aspects of

the disease are described with reference to a few early publications [see also GARAI, this *Bulletin*, 1952, v. 27, 742]. *M. E. Delafield*

RAUSCHKOLB, Ruth R. **Cat-Scratch Disease. A Selective Review.** *Arch. Dermat.* 1959, June, v. 79, No. 6, 674–80. [15 refs.]

ZOONOSES

In this section the abstracts are arranged as far as possible in the following order: General; Anthrax; Brucellosis; Tularaemia; Leptospirosis; Ornithosis; others.

For such tropical diseases as Trypanosomiasis, Leishmaniasis, Rickettsial Fevers, Yellow Fever, Plague, etc., see TROPICAL DISEASES BULLETIN.

ANN. NEW YORK ACAD. SCI. 1958, June 3, p. 70, Art. 3, 277–761, numerous figs. **Animal Disease and Human Health** [LIEBERMAN, James (Conference Chairman)]. [Conference held Sept. 11, 12 and 13, 1957.]

This volume of the *Annals of the New York Academy of Sciences* contains the papers read at a conference on animal disease and human health, held at Atlanta in September 1957. The first part deals with the viral encephalitides—in this instance the anthropod-borne encephalitides. The second part deals with the orphan viruses, and problems of virus diseases of animals. The third part is devoted to leptospirosis and the fourth to rabies. The fifth part relates to ornithosis, the sixth (and longest) to other contemporary disease problems including typhus, Q fever, brucellosis, plague, anthrax and other affections of animals, and the seventh to 2 chronic diseases of animals. The eighth deals chiefly with international programmes and the ninth is a summary.

In each part there are several papers, and these largely summarize work already published, or present the conclusions drawn by the various authors from that work. Most of the speakers were well known American scientists, and their contributions are most valuable in clarifying these complicated subjects. Extensive and useful bibliographies are a feature of these papers.

It is not possible to review such a volume usefully; it should be read in the original by all who are interested in the zoonoses. *Charles Wilcocks*

VERENINOVA, N. K., SMIRNOVA, E. I., KALACHEVA, N. F., KUZNETSOVA, N. I. & KARASEVA, Z. N. **The Effectiveness of Combined Vaccination with Live Vaccines against Plague, Tularaemia, Brucellosis and Anthrax—I. The Compatibility of Live Vaccines (against Plague, Tularaemia, Brucellosis and Anthrax) in an Experiment on Guinea-Pigs.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 11, 1752–9. [12 refs.] [Translated from Russian].

It is not quite clear from the account given what types of strains were used for the preparation of these live vaccines or for the challenge doses in the assessment of the protection afforded by their use; it is assumed that the cultures were attenuated. The combined vaccine containing all four elements appeared to offer a high degree of resistance to guineapigs against infection with organisms of plague, tularaemia and brucellosis but not against anthrax. A monovalent anthrax vaccine induced a high degree of resistance, but in guineapigs inoculated with the combined vaccine the degree of protection against the challenge of anthrax bacilli was negligible. However, if guineapigs were first immunized with a monovalent anthrax vaccine and 10 days later were given a triple-vaccine (plague, tularaemia and brucellosis) the individual protection rates were equal to those induced by monovalent vaccines. *H. J. Bensted*

BENSISSOU, M. & JOUFFREAU. Considérations à propos d'un cas de charbon. [**A Case of Occupational Anthrax: Notes on Prevention**] *Arch. Malad. Professionnelles.* Paris. 1959, May–June, v. 20, No. 3, 301–3.

This short paper contains an account of a case of anthrax in a worker engaged in handling and depilating hides in a leather factory. He noticed the small primary skin lesion in the neck before midday. This increased rapidly in size and by next day there was generalized swelling and oedema of the neck and thorax. The man's temperature was 40°C. Penicillin therapy was carried out with good results.

Several cases of this kind have occurred and the source of infection has been bales of dried or salted hides imported from North Africa or South America. Some figures are given which illustrate the high mortality from occupational anthrax, and the frequency of the head and neck as primary sites of the infection. The hides of goats and kids have been the most frequent sources of infection.

There is a short description of the methods in use for handling and processing the hides. Stress is laid on the importance of special study directed towards preventive measures which should include satisfactory methods for the chemical destruction of anthrax spores. *M. E. Delafield*

PUZISS, M. & WRIGHT, G. G. **Studies on Immunity in Anthrax. VII. Carbohydrate Metabolism of *Bacillus anthracis* in relation to Elaboration of Protective Antigen.** *J. Bacteriology.* 1959, July, v. 78, No. 1, 137–45, 6 figs. [16 refs.]

GARGANI, G. & ALEANDRI, M. La reazione di fissazione del complemento nella diagnosi di brucellosi: indagini su animali da esperimento e su sieri umani, bovini, e ovini. [**The Complement-Fixation Test in the diagnosis of Brucellosis: investigations on laboratory animals and on human, bovine and ovine sera**] *Ann. Sclavo.* Siena. 1959, May–June, v. 1, No. 3, 327–50. [Numerous refs.] English summary.

An extensive, fairly detailed, summary of the literature is given which shows, among other things, a wide

variety in the methods of antigen titration, most workers limiting themselves to estimating complement-fixation activity.

The authors worked on sera of artificially infected rabbits and guineapigs, and on sera from human, bovine and ovine cases. Antigen was prepared from *Brucella melitensis* and *Br. abortus* strains respectively, growing them on potato agar. Suspensions were frozen and thawed for 40 times. Supernatant material, after centrifugation at 6,000–7,000 revolutions per minute, was dialysed through Cellophane and then Seitz-filtered and preserved with 0·4% formalin. These extracts were titrated by chess-board method against rabbit sera, taking the greatest dilution of the antigen which reacted against the greatest dilution of serum as its titre. Haemolysin was titrated against a fixed amount of complement and complement against 2 units of haemolysin. Complement, haemolysin and antigen were used at 10 units per ml., sheep cells being used at 2·5%. A screening test was carried out at $\frac{1}{8}$ dilution.

The complement-fixation test appears to be specific in the serological diagnosis of brucellosis. In rabbits and guineapigs, tests show the necessity of standardizing antigens against the homologous serum, if they are to show relative quantitative differences between *abortus* and *melitensis*. Such differences are apparent in infected and not in vaccinated animals. In naturally infected ovines there were more *melitensis* antibodies, while in bovines there were more *abortus*, which argues for the specificity of the reaction.

The complement-fixation test appears to be more specific but less sensitive and it can serve as a confirmatory test in low-titre agglutinin reactions. The use of hypertonic saline (5%) in agglutination tests gives a greater number of positives. In ovines disagreement between complement-fixation and agglutinin tests is often met with, agreement being better when hypertonic saline is used. In these animals complement-fixation tests, agglutinin reactions and brucellin reactions should be used concurrently. Disagreement also occurs in human cases, the complement-fixation test being sometimes the only positive serological finding in clinically positive cases. *E. Agius*

SIENNICKI, W.; PRZYŁECKI, S.; BASZ, Izabella; CYGANKIEWICZ, Maria; RADZISZEWSKA, Danuta; PIÓRO, Janina. Badania nad brucelozą u ludzi w województwie wrocławskim w latach 1955–1957. Doniesienie I. Bruceloza u pracowników służby weterynaryjnej i zootechnicznej [**Investigations on Brucellosis in Inhabitants of the Province of Wroclaw in 1955–57. Report I. Brucellosis in Workers in the Veterinary and Zootechnical Service**] [SIENNICKI, PRZYŁECKI, BASZ, CYGANKIEWICZ & RADZISZEWSKA]. *Przegląd Epidemiol.* Warsaw. 1959, v. 13, No. 2, 101–11. [23 refs.] Doniesienie II. Bruceloza u pracowników państwowych gospodarstw rolnych [**Report II. Brucellosis in Workers on the State Farms**] [SIENNICKI, PRZYŁECKI, BASZ, CYGANKIEWICZ & RADZISZEWSKA]. *Ibid.*, 113–23. Doniesienie III. Bruceloza wśród pracowników zakładów mleczarskich, rzezni i przetwórstwa miesnego [**Report III. Brucellosis among Employees in Dairies, Slaughterhouses, and Meat-Product Factories**] [SIENNICKI, PRZYŁECKI, BASZ, CYGANKIEWICZ, PIÓRO & RADZISZEWSKA]. *Ibid.*, 125–7.

The English summaries appended to the paper are as follows:—

i "Between April 1955 and December 1956, 603 workers in the Veterinary and Zootechnical Service employed in the districts, treatment centres, slaughterhouses and on the State Farms in the province of Wrocław were examined by the complement-fixation test and the agglutination reaction in a 10 per cent saline solution. A total of 139 veterinary surgeons, 144 veterinary orderlies, 68 veterinary technicians, 210 zootechnicians and 42 inspectors of meat and trichinoscopists were examined. Positive reactions of the serological tests were found in 48 veterinarians (34.5 per cent), 44 orderlies (30.5 per cent), 26 technicians (38.2 per cent), 3 zootechnicians (1.4 per cent), and in 2 meat inspectors (4.7 per cent). In all, therefore, the results of the serological tests were positive in 123 cases. Out of 74 cases with positive complement-fixation reactions the agglutination test was negative in 10 cases, in 34 the titre was 1 : 50 and in 30 the titre was 1 : 100. A titre of 1 : 200 in the agglutination test was found in 18 of those examined. In 16 of these the complement-fixation test was also positive. With positive complement-fixation tests the titre in the agglutination test was 1 : 400 in 22 subjects, 1 : 800 in five and 1 : 1600 in four. In 43 subjects (39.0 per cent) the acute or subacute form of brucellosis was diagnosed, in 25 the chronic form, and in 40 (32.5 per cent) an asymptomatic form. Accurate details are not available for 10 cases (8.2 per cent)."

ii "Between March 1956 and January 1957, 2391 workers employed on the State Farms in the province of Wrocław were examined. Positive results of the serological tests were obtained in 211 (8.8 per cent) of cases. The largest number of cases was recorded in a group of ploughmen (141, i.e. 12.8 per cent), and milkers (51, i.e. 5.4 per cent). At the same time, out of 1013 men examined in the ploughman group, 133 (13.3 per cent) gave positive results and out of 85 women 9 (9.4 per cent). In the milkers, 31 (9.2 per cent) positive results were recorded among the men and 20 (3.3 per cent) among the women. Altogether, in all occupational groups, positive results were obtained in 182 (11.0 per cent) out of 1447 men and in 29 (3.9 per cent) out of 738 women.

"Acute or subacute brucellosis was diagnosed in 30 subjects (14.2 per cent), the chronic form in 26 (12.3 per cent) and an asymptomatic form in 131 (62.1 per cent). In 24 cases (11.4 per cent) it was not possible to determine the clinical form."

iii "Between April and December, 1955, 609 dairy-employees were subjected to the complement-fixation and agglutination tests. Positive results were obtained in only one case, i.e. 0.16 per cent of the total of those examined. In this case, no morbid symptoms were ascertained.

"From March to October, 1957, 1615 workers in slaughter-houses and meat-product factories were

examined. Seven cases of brucellosis were discovered, two of the acute and subacute forms and four of the asymptomatic form. No closer details are available for one case."

SIENNICKI, W. Bruceloza u ludzi w województwie wrocławskim w latach 1950–1957. [**Brucellosis in Inhabitants of the Province of Wroclaw in 1950–57**] *Przegląd Epidemiol.* Warsaw. 1959, v. 13. No. 2, 129–37. [17 refs.]

The English summary appended to the paper is as follows:—

"In the period 1950—57, 405 cases of brucellosis were ascertained among humans. Of this number, 124 cases have been hospitalised with clinical confirmation of brucellosis (123 up to the end of 1957). In particular years, beginning from 1950, the numbers of those admitted to hospital is consecutively 3, 1, 7, 9, 40, 31 and 26. Out of the 405 cases, 45 (11.1 per cent) were women and 360 (88.9 per cent) men.

"Only 20 (4.9 per cent) of these people were town-dwellers, whose occupation had no connection with the rearing of animals or with their products. The remaining 95.1 per cent were people the majority of whom, irrespective of where they lived, had some connection with cattle-raising, the manufacture of animal products or laboratory work.

"As a result of epidemiological enquiries and physical examinations, and on the basis of clinical data, the acute form of brucellosis was diagnosed in 39 cases (9.6 per cent), the subacute form in 59 (14.6 per cent), the chronic form in 69 (17.0 per cent), and the asymptomatic form in 173 (42.7 per cent). There is an absence of closer details as to the remaining 65 cases (16.1 per cent) except that 20 of these were in hospital and so had active brucellosis."

SCHIRGER, A., DEARING, W. H. & WAUGH, J. M. **Intermittent Fever over a 17-Year Period in a Patient with Hypersplenism due to Brucellosis.** *Proc. Staff Meetings Mayo Clinic.* 1959, May 13, v. 34, No. 10, 262–4.

The authors report the case of a man who had suffered from 5 to 6 attacks of fever yearly during a period of 17 years. The fever lasted for a few days only and the patient felt well between the attacks. X-rays showed an enlarged spleen, the leucocyte count was 2,500 per cmm. and the erythrocyte sedimentation rate 62 mm. in 1 hour. Brucellar agglutinins were present in a titre of 1 : 400, a single blood culture was negative. Platelets were not reduced. A spleen about 5 times the normal size was removed and showed necrotic granulomata 3 mm. to 1 cm. in diameter. Culture of the spleen yielded *Brucella suis*. Postoperatively the patient was treated with tetracycline and streptomycin for 4 weeks. Albumin and casts were noted in the urine before the operation. 2 months later the patient suffered from glomerulonephritis after a sore throat 10 days previously.

In comment the authors consider recurrent fever not especially common in non-bacteraemic brucellosis. The long duration, 17 years, exceeds by 3 years the case reported by OSMUNDSON *et al.* [this *Bulletin*, 1957, v. 32, 662]. [The term non-bacteraemic scarcely seems justified on the basis, apparently, of 1 negative blood culture. The indication for splenectomy before a trial of antibiotic therapy is not clear to the reviewer. MANSON-BAHR in the list of references is mis-spelt Mason-Bahr]. *Frederick J. Wright*

MOLINELLI, E. A., VERA BARROS, E. & ITHURRALDE, D., with the technical assistance of Emma M. CAUBISENS POUMERAU & F. ROSSI. **Tetracycline-Oleandomycin in Human Brucellosis Therapy. Preliminary Observations.** Reprinted from *Antibiotics Annual 1957–1958.* pp. 692–7, 2 figs. 1958. New York: Medical Encyclopedia, Inc., N.Y.

The authors record the results of treating 6 patients suffering from brucellosis with a 2 : 1 mixture of tetracycline and oleandomycin. (This mixture has the trade name of Signemycin.) Preliminary laboratory work had demonstrated bacteriostatic activity against *Brucella abortus*, *Br. suis* and *Br. melitensis* in concentrations ranging from 0·23 to 1·98 μgm./ml. and bactericidal activity after 1 week's incubation at a concentration of 31 μgm./ml. Acquired resistance was not observed. All the 6 patients were treated with 3 gm. of the tetracycline and oleandomycin mixture daily, in 6-hourly divided doses for 14 days. 4 received, in addition, prednisolone 5 mgm. every 6 hours to totals of 50–60 mgm. in the first 60–72 hours of treatment. All showed a quick defervescence of fever (3 to 72 hours). Low-grade Herxheimer-like reactions were observed in the 2 not receiving prednisolone. Side-effects were absent or mild. There were no relapses during periods of observation from 21 to 105 days after treatment. [These results are encouraging and warrant further trial and more prolonged follow-up observation.] *Frederick J. Wright*

FYVIE, A., ROSS, W. G. & LABZOFFSKY, N. A. **Tularemia among Muskrats on Walpole Island, Lake St. Clair, Ontario.** *Canadian J. Comp. Med.* 1959, May, v. 23, No. 5, 153–6, 1 fig.

The authors report an epizootic among muskrats due to *Brucella tularensis* isolated both from splenic tissue of muskrats and from the mud and very stagnant water in which the dead muskrats were found. The isolation of *Br. tularensis* from water has been previously reported by others and suggests the possible importance of contaminated water in the spread of tularaemia and raises the question as to whether *Br. tularensis* can multiply in such a medium. *Frederick J. Wright*

DOLD, H., JORDAN, G., MERKER, H., SCHMID, F. & SJÖSTEN, H. Eine Feldfieberepidemie mit epidemiologischen Besonderheiten. [**An Epidemic of Leptospiral Disease (Mud Fever) with Special Epidemiological Features**] *Deut. med. Woch.* 1958, Dec. 26, v. 83, No. 52, 2322–5, 2355. [11 refs.]

Epidemics of infection by *Leptospira grippotyphosa* normally affect predominantly agricultural workers, and are most likely to occur at harvest-time in years

when the carrier rodents are plentiful, the weather is warm and the fields are water-logged by heavy rain. The epidemic described here occurred during the hot summer of 1952, but the weather was dry, most of the patients were between 10 and 16 years old, and a history of bathing in a particular stream was obtained in nearly every case. Serological tests showed that the infections were caused by *L. grippotyphosa.*

Of 16 *Microtus arvalis* trapped in the vicinity 4 had positive agglutinin titres for *L. grippotyphosa.* No strains of leptospires were isolated from kidney cultures possibly, as the authors suggest, because the media used were prepared with chlorinated tap water.

J. C. Broom

MATEEW, D. Die Leptospirosen in Bulgarien. [**The Leptospiroses of Bulgaria**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1959, Jan.–Feb., v. 5, No. 1, 45–55. [Numerous refs.]

Leptospirosis was first recognized in Bulgaria in 1944 when there was an epidemic of classical Weil's disease in a military camp reported by OSTERTAG [this *Bulletin*, 1951, v. 26, 147]. This article gives a summary of investigations, made by the author and a number of other workers, of the incidence of leptospirosis in man and domestic animals in recent years. It is now apparent that leptospirosis is widespread in Bulgaria and a number of epidemics occur annually. These are mainly caused by *Leptospira pomona* and the disease is commonest among adolescents who have bathed in streams liable to pollution by pig urine.

Strains isolated in culture from human cases were identified as *L. bataviae, L. grippotyphosa, L. hyos, L. icterohaemorrhagiae* and *L. pomona.* Other strains isolated were given the names *L. benkovski, L. nikolaevo, L. plovdiv* and *L. tzalapitza.* The last appears to be closely related to *L. pomona,* and *L. plovdiv* was later found to be identical with *L. mini.* The antigenic affinities of the other "serotypes" have not yet been investigated.

Serological tests on man and domestic animals suggest that the following serotypes are also probably present in Bulgaria: *L. australis A, L. australis B, L. canicola, L. hebdomadis, L. saxkoebing* and *L. sejroe.*

[There has been a regrettable tendency in recent years for workers to give names, which suggest they represent new serotypes, to strains whose serological characteristics have not been fully investigated. Such precipitancy inevitably leads to confusion, as in the case of *L. plovdiv* which proved to be *L. mini.* The difficulty could be overcome by sending cultures of "new" serotypes to one of the WHO/FAO Leptospirosis Laboratories which are prepared to make these investigations. The addresses of these laboratories are published in World Health Organization Technical Report Series, No. 169. Joint WHO/FAO Expert Committee on Zoonoses, Second Report, (1959) p. 72.

The addresses are: AUSTRALIA, Laboratory of the Queensland Department of Health and Home Affairs. Brisbane, Queensland; ITALY, Istituto Superiore di Sanità, Viale Regina Elena 299, Rome: JAPAN, Department of Viral and Rickettsial Diseases, National Institute of Health, Tokyo; NETHERLANDS, Institute for Tropical Hygiene and Geographical Pathology (Royal Tropical Institute), Mauritskada 57 A, Amsterdam; UNITED KINGDOM OF GREAT BRITAIN AND NORTHERN IRELAND, The Wellcome Laboratories of Tropical Medicine, 183, Euston Road, London, N.W.1; UNITED STATES OF AMERICA, Division of Veterinary Medicine, Walter Reed Army Institute of Research, Walter Reed Army Medical Center, Washington 12, D.C.]

J. C. Broom

VYSOTSKII, B. V., MALYKH, F. S. & KUZNETSOV, A. P. **Fur-Bearing Animals as Additional Reservoirs of Pathogenic Leptospires in the Wild.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 8, 1227–9. [Translated from Russian.]

A serological survey of fur-bearing animals was made to obtain information about their possible role in transmitting leptospirosis to man. Agglutinins were found in the blood of 9 species—ussurian tiger (1/2), spotted deer (42/429), wolf (6/21), fox (57/81), ussurian raccoon (30/63), mink (10/79), squirrel (2/10), muskrat (21/365) and Karako rat [*Rattus norvegicus caraco*] (3/52). Agglutinins for *Leptospira hyos* and *L. pomona* were found only in spotted deer which are being domesticated and so come into contact with cattle. A few members of all species (to a total of 19) except tiger, deer and squirrel reacted with *L. grippotyphosa.* One or more individuals of all species were positive with *L. nero,* the highest rates being 70·4% in foxes and 46·6% in raccoons. [*L. nero* belongs to the Hebdomadis serogroup (see KRAMINSKAYA, this *Bulletin,* 1957, v. 32, 325) and is mainly carried by *Microtus oeconomus* and *M. fortis,* but no details of its serological characters have been published so far as the reviewer is aware.]

Marshy ground is the favourite habitat of raccoons which may therefore infect water frequented by man. [MCKEEVER *et al.* (*ibid.,* 1959, v. 34, 538) suggested that raccoons might have been responsible for the epidemics of Fort Bragg fever which occurred in the U.S.A. in the summers of 1942–44.] The handling of infected animals obtaining pelts for the fur industry may also provide a means for the transmission of leptospirosis to man.

J. C. Broom

ESKIN, V. A., KRAMINSKAIA, N. N., BERKUT, I. B., IRLIN, S. P. & IZOTOV, P. V. **Epidemiological and Clinical Features of Ussurian Leptospirosis.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 8, 1233–40, 2 figs. [Translated from Russian.]

Certain strains of leptospires isolated from patients suffering from acute febrile illnesses were considered to belong to a new serotype which was named *Leptospira ussuri.* [No details are given of the serological characters of this serotype, nor it is stated with which other serotypes it was compared.] During the hot wet summer of 1955 an epidemic of 159 cases due to this serotype occurred among the rural population in the Primorskii province of Siberia, and in the following year, when the weather was cooler and drier, there was a smaller outbreak of 49 cases. The disease was almost certainly contracted by contact with infective water, and the incubation period could be reliably

established for 50 patients who had been at risk only on one occasion. The average incubation period was 14·1 days with a range from 7–21 days.

The disease was relatively mild in character and all the patients recovered. Treatment with penicillin appeared to suppress the symptoms provided it was given early. The usual course was 200,000–300,000 units intramuscularly every 4 hours for 6–7 days. With lower doses or a shorter course there was a recrudescence of fever and symptoms.

Some of the haematological findings differed from those generally present in other benign forms of leptospirosis. During the first few days the erythrocyte sedimentation rate was 5–10 mm. in the first hour. The rate increased somewhat between the 4th and 10th day but rarely exceeded 20–25 mm. and it returned to normal at the end of the febrile period. The leucocyte count was generally below normal though there was a relative neutrophilia of 70–85%. *J. C. Broom*

COCHAVY, Z. **The Epidemiology of Leptospirosis in Man in Israel 1949–1957.** *Harefuah.* Jerusalem. 1959, July 15, v. 57, No. 2 [In Hebrew 31–4, 9 figs. (13 refs.) English summary 35].

The English summary appended to the paper is as follows:—

"1. The present epidemiological survey is based on 640 cases reported to the Ministry of Health during the period 1949—1957.

"2. Of 130 cases reported since 1953, 96 were due to *L. grippotyphosa*, 31 to *L. canicola*, and 3 to *L. icterohemorrhagiae*.

"3. The epidemic curve shows a peak in late summer and early autumn in each of the past 5 years. The coastal plain and the central area of the country provided the majority of the cases. The age incidence was between 15 and 65. 81% of all cases were males.

"4. Analysis of occupations showed that more than half of the cases were engaged in agriculture and the tending of cattle and pigs. This parallels the known high prevalence of leptospirosis infections amongst sheep, goats, dogs, pigs and bovines.

"5. Clinical symptoms are characterised by fever, chills, muscular aches, severe malaise and vomiting. Common complications are conjunctivitis and iridocyclitis. 102 cases were hospitalized, the average stay being 18 days.

"6. The most efficient preventive methods of limiting the spread of the disease in man in Israel are: Rodent control, immunization of those in hazardous occupations, environmental sanitation of farm yards and barns, adequate handling, keeping and treating of healthy livestock, annual examination of domestic dogs and destruction of all stray dogs, as well as the wearing of suitable footwear by agricultural workers."

WOLFF, J. W., COLLIER, W. A., BOOL, P. H. & BOHLANDER, H. **Investigations on the Occurrence of Leptospirosis in Surinam.** *Trop. & Geograph. Med.* Amsterdam. 1958, Dec., v. 10, No. 4, 341–6, 1 chart.

Human cases of leptospirosis had been diagnosed in Surinam on clinical evidence for a number of years, but no serological confirmation was obtained until 1951. In that year a sample of serum from a patient with symptoms suggestive of benign leptospirosis was tested at Amsterdam and gave positive agglutination reactions with *Leptospira grippotyphosa*. A second case, also mud fever, was confirmed serologically in 1955, and a strain of leptospires, isolated from a third, fatal case in 1956, was identified as *L. icterohaemorrhagiae*.

Samples of serum from some 700 domestic animals (mainly cattle, pigs and dogs) and 175 rats [species not stated] were tested against a range of 14–17 serotypes of leptospires. Agglutinin titres of 1 in 100 or more were regarded as indicative of infection. *L. icterohaemorrhagiae* was predominantly the serotype involved—61 out of 82 positive reactions. However, of the 199 cattle tested, roughly equal numbers of the 14 positive reactors had agglutinins for *L. icterohaemorrhagiae*, *L. autumnalis*, *L. pomona*, *L. grippotyphosa*, *L. hebdomadis*, *L. sejroe* and *L. bataviae*. Strains of leptospires isolated from 20 *Rattus norvegicus* and 1 dog were identified as *L. icterohaemorrhagiae*. *J. C. Broom*

KLEINSCHMIDT, A. & CHRIST, P., with the assistance of G. KREUZ. *Leptospira ballum* als Ursache einer Laboratoriumsinfektion. [**A Laboratory Infection caused by** *Leptospira ballum*] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, Feb., v. 117, No. 2, 107–13. [25 refs.]

A laboratory worker was bitten on the hand by a white mouse and the wound was contaminated with urine. After 8 days the site became swollen and painful but there was no sign of sepsis. On the 12th day the man had a sudden febrile attack and developed symptoms suggestive of leptospirosis. Leptospires were isolated by blood culture and proved to be *Leptospira ballum* subtype (AB), first described by BABUDIERI [this *Bulletin*, 1956, v. 31, 1043]. The same subtype was isolated from the mouse.

This patient did not develop orchitis which was a common symptom in the cases of *L. ballum* infection reported by STOENNER and MACLEAN [*ibid.*, 1958, v. 33, 749]. *J. C. Broom*

CHOLVIN, N. R., MORSE, E. V. & LANGHAM, R. F. **Experimental** *Leptospira pomona* **Infections in Dogs.** *J. Infect. Dis.* 1959, Jan.–Feb., v. 104, No. 1, 92–100, 3 figs. [28 refs.]

8 dogs were inoculated with a strain of *Leptospira pomona* which was virulent for guineapigs and hamsters, and 4 other dogs were fed with carcases of guineapigs killed during the leptospiraemic stage of infection. Positive blood cultures were obtained from all the inoculated dogs between the 4th and 7th days; none of those fed on infective material yielded cultures but leptospires were present in the urine of one dog in this group between the 21st and 32nd days and were demonstrated in its kidneys when it was killed on the 54th day. The other 3 never showed any evidence of infection.

Leptospires were detected in the urine of 5 of the dogs infected by inoculation on various occasions

between the 14th and 47th days but not later. Kidney infections were demonstrated in 2 of these dogs killed respectively on the 21st and 26th days.

None of the dogs showed any clinical symptoms, but at autopsy scattered white foci were present in the renal cortex and extending into the medulla. Microscopical examination revealed interstitial nephritis with an infiltration of lymphocytes and plasma cells and degeneration of the tubular epithelium.

Since leptospiruria can occur after oral exposure to *L. pomona*, dogs may on occasion be responsible for transmitting this infection to other animals or to man. However, in view of the short period during which they excrete leptospires it seems unlikely that dogs are important reservoir hosts of this serotype.

J. C. Broom

LANG, R. W. & MORSE, E. V. **Serologic Cross Reactions among Leptospirae observed with Sera from Animals infected with** *Leptospira pomona*. *J. Immunology*. 1959, May, v. 82, No. 5, 471–6, 4 figs. [17 refs.]

A comparison was made of the antibody responses elicited in different animal species, experimentally infected with either of 2 virulent strains of *Leptospira pomona*. Sera were taken at frequent intervals from 17 sheep, 9 pigs, 4 goats and 30 guineapigs and their agglutinin titres tested against *L. pomona*, *L. canicola*, *L. icterohaemorrhagiae* (AB) and *L. icterohaemorrhagiae* (A). Although there were minor differences [full protocols are given in the original] the sheep, goats and pigs responded very similarly. The agglutinin titres for *L. pomona* rose steeply during the second week and were still at a high level at the end of the periods of observation—88 days for the sheep, 39 for the goats and 83 and 152 days respectively for 2 groups of pigs. The rise and persistence of titres for the heterologous serotypes were roughly parallel to those for *L. pomona* but their levels were always much lower.

[There were apparently none of the "paradoxical reactions", not uncommon in human sera, in which heterologous titres may be higher than the homologous titre during the early states of infection; see FÜHNER, this *Bulletin*, 1951 v. 26, 607.]

In guineapigs, agglutinins developed for *L. pomona*, *L. canicola* and *L. icterohaemorrhagiae* (A) and persisted for at least 60 days, but the titres were much lower. For *L. pomona* it reached only about 10^{-4} as compared with 10^{-8} to 10^{-9} in the domestic animals.

Agglutinin absorption tests were made with the sera of 1 sheep and 2 pigs, and the results obtained with one serum [extracted from the authors' Table] are shown below. [These results are most surprising in that absorption with *L. icterohaemorrhagiae* reduced the homologous antibody levels to 5% and 1% respectively for the 2 strains of *L. pomona*. The abstracter's experience of absorption tests is admittedly limited to work with antisera from immunized rabbits and human cases of leptospirosis. After absorption such sera may react to one dilution less than before, but nothing approaching the reductions in titre reported here has ever been encountered. It would be of great interest to know whether similar results have been obtained with sera from other animals.]

J. C. Broom

Agglutinin Absorption Results with *Leptospira pomona* antiserum

Serum from Pig No. 1, 59 days after exposure	*Titres against antigens*				
Absorbing serotype	*L. pomona* (Wickard)	*L. pomona* (Johnson)	*L. ictero.* (AB)	*L. ictero.* (A)	*L. canicola*
None	1,000,000	50,000,000	500	500	1,000
L. pomona	0	0	0	0	0
L. ictero-haemorrhagiae (AB)	50,000	500,000	0	0	0

0 = Negative at serum dilutions of 1/10 upwards.

TERZIN, A. L., HLACA, D. M. & FORNAZARIC, M. R. **Antibodies against Bedsonia Antigen in Sera of Animals.** *Arch. f.d. gesamte Virusforschung*. 1958, v. 8, No. 4, 511–26. [23 refs.]

With the object of obtaining an indication of the prevalence of infection with viruses of the psittacosis group in certain species of birds and mammals in Yugoslavia, the authors have examined sera collected from 502 birds and beasts in Bosnia, Croatia and Northern Serbia. 251 birds were sampled: 104 pigeons and 147 other species (goose, duck, turkey, domestic fowl); the remaining 251 sera were from sheep, cattle and horses. Both direct and indirect complement-fixation tests with the heat-stable group antigen were made with each serum which were invariably titrated to an end point; complete fixation or inhibition of fixation at a dilution of at least 1 in 4 was accepted as positive. From 20 to 65% of the pigeons were seropositive, in some the titre being very high; the highest observed was 1 in 16,384. Some of the pigeons were kept in captivity making more than one observation possible in the same bird and in some of these a fall in titre, or even the disappearance of antibodies, occurred in the period of observation of 400 days. The incidence of positive reactors in other birds varied from 22% in domestic fowls to 55% in geese. The titres observed in mammals were less than those found in birds. 22 out of 82 sheep possessed antibody and 38 of 155 cattle were positive as were 5 of 14 horses.

S. P. Bedson

RINDGE, Mila E., JUNGHERR, E. L. & SCRUGGS, J. H. **Serologic Evidence of Occupational Psittacosis in Poultry-Plant Workers.** *New England J. of Med.* 1959, June 11, v. 260. No. 24, 1214–18.

The occurrence of a case of psittacosis in a middle-aged woman in Connecticut, who in the 18 months before her illness had been employed on a poultry processing plant, led to the Connecticut State Department of Health making a serological survey of the employees on a number of poultry processing plants in this State. Of 109 employed on 6 plants 24 possessed antibodies for the psittacosis group of viruses and 8 of these gave titres of 1 in 16 or more (acute reactors); those with lesser titre were designated "reactors". Reactors were found only among "eviscerators" and the majority of those with the higher antibody titres ("acute reactors") gave a history of upper respiratory illness. *S. P. Bedson*

Diseases due to Fungi

For papers on systematic mycology, see the section in Bacteriology, below. Papers on Blastomycosis (South American type), Coccidioidomycosis, Mycetoma and Rhinosporidiosis are abstracted in the TROPICAL DISEASES BULLETIN

CATANEI, A. Sur trois champignons agents de teignes humaines au Sahara. [**Concerning Three Fungi Causing Human Ringworm in the Sahara**] *Arch. Inst. Pasteur d'Algérie.* 1959, Mar., v. 37, No. 1, 55–60. [12 refs.]

Brief clinical and mycological notes are given in the case of 3 types of tinea capitis infection as well as notes on their geographical distribution in the Algerian Sahara. They are all species of *Trichophyton*, namely, *T. soudanense*, *T. pervesi* and *T. langeroni*. Although *T. soudanense* is only 1 of 4 species causing tinea capitis in the Algerian Sahara it ranks second to *T. violaceum* as the most common aetiological agent of this disease. It shows no predilection as regards race. Children are most susceptible to infection by it between the ages of 5 and 10 years. The lesions caused by it in the scalp are variable. They may be few or numerous, and present as small patches which are scaly or furfuraceous, or as large and ill-defined scaly patches; crusts may also be present. Infection in adults can occur. Superficially, infected hairs do not differ from hairs infected by other species of *Trichophyton*, but they reveal an endothrix arrangement of the fungus. The cultural features of this species have already been described by VANBREUSEGHEM [this *Bulletin*, 1951, v. 26, 496 and 642]. *T. pervesi* occurs about 7 times less frequently than *T. soudanense* as the aetiological agent of tinea capitis. In the hair it presents as an endothrix-type of *Trichophyton*; in culture its surface growth is folded, powdery and violaceous with cracks at the centre; its margin is radiating. *T. langeroni* was first isolated from an Algerian camel in 1930 but the present strain was isolated from a kerion lesion in a Mussulman boy who had been in contact with a goat suffering from ringworm caused by the same species. The pattern which it presented on the hair was that of an ectothrix megaspore *Trichophyton*. *C. J. La Touche*

DOBY-DUBOIS, M., DOBY, J. M. & DEBLOCK, S. Complément à l'étude des teignes du Cameroun. II. Étude statistique et épidémiologique. [**Further Observations on Tinea in the Cameroons. II. Statistical and Epidemiological Study**] *Bull. Soc. Path. Exot.* 1958, Nov.–Dec., v. 51, No. 6, 935–41, 4 graphs.

COCHET and DOBY-DUBOIS (1957) and COCHET *et al.* [this *Bulletin*, 1958, v. 33, 661] reported the mycological results of a study of 866 infections of the hair in 2,984 children in the region of Yaoundé (Cameroons). In this paper the authors make a statistical and epidemiological study of the data.

Between the ages of 4 and 10 years, more than one-half the population carry mycotic lesions; probably at one time in their lives practically everyone becomes infected. Interesting differences are found in the rates of infection with the different organisms in the villages and in the town of Yaoundé itself and in the 3 main tribal groups, Bantus, Hausas and Bamilekes at different ages. *Peter Abbott*

BAYLET, R., HUBERT & QUENUM, C. Index histoplasmique en A.O.F. [**Histoplasmin Index in French West Africa**] *Bull. Soc. Path. Exot.* 1958, July–Aug., v. 51, No. 4, 582–9.

678 adult Africans from different territories of French West Africa (A.O.F.) were tested with intradermal histoplasmin (and, at the same time, tuberculin) with the object of investigating the incidence and distribution of histoplasmosis. The overall incidence of positive reactors was 9% but figures ranged from 28% reactors from the Ivory Coast to 1·5% in Senegal and 0 out of 14 in Dahomey. The biological peculiarities of the areas of high endemicity are considered in some detail with particular mention of the caves which are found there.

47% of those tested showed positive reactions to tuberculin; cross-reaction with histoplasmin was not observed with the dosage used. *Peter Abbott*

SASLAW, S. & BEMAN, F. M. **Erythema Nodosum as a Manifestation of Histoplasmosis.** *J. Amer. Med. Ass.* 1959, July 4, v. 10, 1178–9. [14 refs.]

This report of a case of erythema nodosum associated with histoplasmosis concerns an 18-year-old girl from Copenhagen who had arrived in the United States 3 months previously to enrol at the Ohio State University. As part of the programme at this University she submitted to various skin sensitivity tests which included both purified protein derivative (PPD) and histoplasmin. Her tuberculin test was positive and the histoplasmin test negative. Her chest X-ray was normal. On admission to hospital her physical findings were, on the whole, normal, except for a bilateral conjunctivitis and the aforementioned erythema nodosum which manifested itself as raised, nodular, erythematous, tender lesions, measuring 2–4 cm. in diameter, on both legs. Her blood picture revealed the following features: white blood cell count, 11,400 per cmm. with 71% neutrophils, 23% lymphocytes, 4% eosinophils and 2% monocytes; the haematocrit value was 43% and the haemoglobin level was 13·6 gm. per 100 ml. Urinalysis revealed no abnormality and throat culture was negative. The streptolysin and heterolysin agglutination tests were also negative.

The yeast-phase complement-fixation test for histoplasmosis was negative, but the histoplasmin collodion agglutination test was positive with a titre of 1 in 40, and the histoplasmin skin test was positive with induration and oedema measuring 30 mm. in diameter after 48 hours. Also, a second PPD test gave a positive result and this time the chest X-ray revealed a mild bilateral adenitis and some evidence of pneumonitis in the medial segment of the middle lobe of the right lung. The collodion agglutination test on being repeated 1 week later gave again a positive result, again with a 1 in 40 titre, but the complement-fixation tests remained negative. A single bone-marrow culture and 3 blood cultures gave negative results. Treatment was symptomatic and the patient remained afebrile throughout. She was discharged on the thirtieth day after admission, by which time the lesions on her legs were less painful and somewhat darker and smaller.

Histoplasmosis is endemic in the East Central United States which include the State of Ohio, so that the patient was liable to succumb to infection sooner or later. Erythema nodosum is already known to occur in cases of coccidioidomycosis, and, in the authors' opinion histoplasmosis may yet be another disease giving rise to this syndrome. The negative results obtained on culture and with the complement-fixation test are, according to their previous experience, not inconsistent with a diagnosis of histoplasmosis.

C. J. La Touche

FELSON, B. **Some Less Familiar Roentgen Manifestations of Intrathoracic Histoplasmosis.** *Arch. Intern. Med.* 1959, Jan., v. 103, No. 1, 54–62, 5 figs. [30 refs.]

"Histoplasmosis has become increasingly prominent as a cause of intrathoracic pathology, chiefly because of a greater alertness to its presence. The variety of intrathoracic roentgen patterns encountered in this disease is also increasing as experience accumulates. The present report deals with some less familiar roentgen manifestations of histoplasmosis, including the fibrocavitary form, enlarging histoplasmoma, large multinodular lesions, and certain sequelae of long-standing histoplasmic lymphadenitis, such as broncholithiasis, traction diverticulum of the esophagus, the middle lobe syndrome, and superior vena caval obstruction. In the endemic area the disease must be given serious consideration in all instances in which a diagnosis of pulmonary tuberculosis was formerly entertained."

SEGAL, E. L., STARR, G. F. & WEED, L. A. **Study of Surgically Excised Pulmonary Granulomas.** *J. Amer. Med. Ass.* 1959, May 30, v. 170, No. 5, 515–22, 6 figs.

In a large percentage of pulmonary granulomas excised in the Mayo Clinic over a period extending from 1946 to 1956 an aetiological agent could not be demonstrated by routine staining procedures. In January 1956 the authors decided to use Gomori's methenamine-silver nitrate stain (GMS) in their future investigations of granulomas. The use of this stain for the purpose of demonstrating pathogenic fungi in tissues was described by GROCOTT in 1955 and this method has since been gaining rapidly in popularity. A total of 138 granulomas were stained in this manner by the authors.

Results showed that more than one-half (55·9%) of the granulomas contained structures resembling either *Histoplasma capsulatum* or *Coccidioides immitis* although cultures had proved negative. In one-fourth of the total number investigated cultures were positive, and in approximately one-fifth both culture and microscopical examination after staining by GMS failed to reveal an aetiological agent. The results compared very favourably with those obtained before 1956, and accordingly, the authors are satisfied that the GMS stain is superior to other stains for use in these investigations in so far as it is able to reveal the presence of non-viable organisms which could not be detected by other known stains. The authors nevertheless take care also to point out the limited value of improved staining procedures in diagnosis in the absence of positive cultures, however effective they might prove to be in revealing microscopically otherwise undetectable organisms. *C. J. La Touche*

STEIN, A. A. **Systemic Moniliasis: A Clinicopathological Report of Five Cases.** *Antibiotic Med.* New York. 1959, May, v. 6, No. 5, 297–308, 6 figs. [25 refs.]

In these days of antibiotic medicine it has become almost a habit of mind for the clinician to be on the alert for the possible development of mycotic infection in the patient to whom he is administering a course of antibiotics. In fact, when fungal infection does

develop in such a patient the instinctive reaction of some clinicians is to withhold further administration of the antibiotic until the fungal infection will have been brought under control.

The author of this article is of the opinion that it is a false assumption that prolonged antibiotic therapy may be responsible for precipitating systemic *Candida* infection although he concedes that such therapy tends to promote surface growth of this organism, for instance, on the oral mucosa. He stresses instead the traumatic element in the presence of active *Candida* growth as the precipitating factor in these cases.

In support of his contention he proceeds to describe in this well-illustrated article the clinical course and pathological features of 5 cases of generalized infection by species of *Candida*, in each of which he was able to locate a traumatic portal of entry to the general circulation for these pathogens. All of these patients succumbed to systemic infection by *Candida* only when they were in an extreme state of debility in the terminal stages of the primary disease from which they were suffering. Antibiotics were administered in all cases. In 2 of the patients ulceration of the oral mucosa was associated with the presence of active *Candida* on the mucosa; in 1 a toothpick was found to have perforated the duodenum; in another there were acute ulcerations of the jejunal mucosa in the presence of *Candida* growth; and lastly, in one, a recently performed cholecystectomy had resulted in postoperative complications of a surgical nature.

C. J. La Touche

Kozinn, P. J., Wiener, H., Taschdjian, Claire L. & Burchall, J. J. **Is Isolation of Infants with Thrush Necessary?** *J. Amer. Med. Ass.* 1959, July 4, v. 170, No. 10, 1172–4. [13 refs.]

The results of a 6-month investigation of thrush among 1,622 newborn infants have convinced the authors of this article that such precautions against spread of infection as isolation or segregation of affected individuals or contaminated nursing personnel are not effective measures in reducing the incidence of this disease. During this 6-month investigation 3 isolation periods alternated with 3 segregation periods. During the isolation periods 786 babies with oral thrush confirmed by direct smears and cultures were sent to an isolation nursery, and during the segregation periods 836 such patients were segregated to one side of a general nursery. Oral smears and cultures were taken from every infant on the third day of birth and repeated on the seventh day. The babies remained in the hospital for an average of 8 days in the case of female infants and for 9 days in the case of male infants. Clinical thrush usually manifested itself by that time. On the 16th day information was obtained from the mother as to whether the baby had developed thrush or not, and all suspicious cases were investigated as soon as possible.

Data collected included: location of infected babies relative to healthy babies in the nursery, observation of babies attended by nurses tending babies with thrush, and, as a check on the possibility of spread by droplet infection, exposure of Petri dishes containing Sabouraud's agar for 24 hours, in the immediate vicinity of patients. "Infected infants were classified into three categories: (1) clinical thrush—infants who developed clinical oral thrush while in the hospital; (2) latent thrush—infants who yielded *Candida albicans* on culture while in the hospital, but did not develop clinical manifestations up to the 16th day of life; (3) delayed thrush—infants who developed clinical oral thrush between the day of discharge and the age of 16 days."

Observations as regards periods of exposure of babies to possible infection showed that babies in the segregation and isolation categories who did develop thrush were exposed for approximately the same period as babies who did not develop thrush. Results also showed that, although exposure to clinical thrush for the isolation groups was only one-half as long as that for the segregation groups the incidence of infection was almost twice as high as that in the segregation groups. As regards infants who were not exposed to clinical thrush while in the nursery (23·5% of the total number) the incidence of clinical and latent thrush was higher in this than in the previous groups. Furthermore, no yeast colonies were observed on the Petri dishes after incubation.

From these observations the authors reach the important conclusion that isolation procedures do not reduce the incidence of thrush in nurseries and that the cost entailed in carrying them out is therefore not justified. Finally, they stress the importance of treatment of vaginal thrush in the mother during the last 3 months of pregnancy before term since they are convinced that the majority of babies who contract candidiasis do so at birth. [In this connexion it seems unfortunate that the authors did not themselves take vaginal swabs for culture from the mothers after or before they gave birth to the babies who were the subject of this survey, as the results of such cultures might have provided significant confirmatory evidence for their conclusion. The possibility of carriers among the nursing personnel might also have been investigated with interesting results.]

C. J. La Touche

Larsen, Martha C., Diamond, H. D. & Collins, H. S. **Nocardia Asteroides Infection. A Report of Seven Cases.** *Arch. Intern. Med.* 1959, May, v. 103, No. 5, 712–25, 5 figs. [17 refs.]

"Seven cases of infection due to *Nocardia asteroides* are presented. In 5 there was coexisting neoplastic disease. In this group of cases of nocardiosis, cure in three instances was associated with surgical extirpation of the infectious lesion. Death was considered due primarily to nocardiosis in two of the cases, to cancer in two others.

"The detection of nocardiosis in the cases with cancer was frequently difficult, and the pathogenesis of the infection obscure. This is attributed in some instances to the presence of neoplastic disease, in others possibly to the use of long-term therapy with corticotrophin (ACTH), cortisone or prednisone and its attendant alterations in host response.

"No recommendation as to antimicrobial therapy of

choice can be made on the basis of the cases described. Antibiotic therapy alone was not conspicuously sucessful in eradicating the infection, despite hopeful expectations based on tests in vitro of sensitivity. Suppression of the infection was achieved in several instances. The accumulated literature now suggests the sulfonamides might have proved more effective and should have been used.

"Tests for sensitivity to various antibiotics in vitro of the strains of Nocardia isolated from these seven cases suggests that variations in strains not discerned by the standard procedures of determinative bacteriology may be detected by this means."

BORLAND, D. S. **Mucormycosis of the Central Nervous System.** *J. Dis. Children.* Chicago. 1959, June v. 97, No. 6, 852–6 3 figs. [14 refs.]

A fatal case of mucormycosis of the central nervous system is described in a 7-month-old Negro boy after a severe gastro-intestinal upset which resulted in marked acidosis. On admission he was severely dehydrated and was suffering from shock. The right eye was bulging and the right eyelid was swollen. The right pupil did not react to light. The left eye appeared normal. Among laboratory data a noteworthy feature was a white blood-cell count of 22,000 per cmm. Despite the administration of several antibiotics the patient's condition deteriorated rapidly. 3 days before death a black necrotic area appeared on the nasal side of the right eye and this increased in area to involve the forehead and the bridge of the nose (illustrated photographically). Cultures from the right eye during life yielded only a scant growth of haemolytic *Staphylococcus aureus*. 2 blood cultures and a spinal fluid culture were negative.

At autopsy the following main gross pathological features were recorded: the skin within the black area already noted was black and gangrenous and the soft tissue of the orbit was soft and necrotic; the brain was extensively soft, only the pons and cerebral hemispheres retaining some semblance of normal shape and consistency. There was evidence of fresh haemorrhage suggesting infarction; the meninges and blood vessels at the base of the brain were covered with a purulent exudate and the blood-vessels appeared to be thrombosed. The ethmoid and the bones around the orbit were soft and necrotic; the right cavernous sinus was filled with a grey putty-like material. Examination of microscopical preparations of affected tissues revealed extensive proliferation of a mucoraceous-type mycelium in the nasal bones and soft tissues as well as in the right eye and right orbit. It was also abundant in those areas of the brain and meninges which were involved (photographs shown) in the pathological process. The mycelium appeared to have a particular affinity for the blood-vessels almost all of which were thrombosed. No other organs were invaded by the fungus but the kidney revealed signs of the severe septic process present in the eye and brain. The chief feature in which this otherwise typical case differed from previously described cases of mucormycosis was the absence of any evidence of diabetes, but in common with them acidosis was a marked feature. Unfortunately, no cultures were made at autopsy thus precluding exact identification of the aetiological agent.

C. J. La Touche

See also p. 1125, UYTERLINDE, [**"Farmer's Lung", an Acute Pulmonary Disease due to Threshing Mouldy Grain**].

See also p. 1125, FREYTAG *et al.*, [**Dust Concentration during Threshing Work and Investigation of the Microflora of the Dust**]

See also p. 1125, PESTALOZZI, [**Febrile Disease in Carpenters in a Carpentry Works through Inhalation of Moist Air Contaminated by Moulds**].

Rheumatic Diseases

MCEWEN, C. **Current Status of Therapy in Rheumatic Fever.** [Report to the Council on Drugs (KAUTZ, H. D., Secretary).] *J. Amer. Med. Ass.* 1959, June 27, v. 170, No. 9, 1056–62.

This is a report on current findings in the treatment of rheumatic fever authorized by the Council on Drugs of the American Medical Association. The following points are made:

(1) It is now definitely established by streptococcal antibody tests that group A haemolytic streptococci play an essential role in the causation of rheumatic fever. Highly important advances have been made in the prevention of rheumatic fever by (a) continuous prophylaxis with sulphonamides or penicillin for many years, and (b) by early penicillin therapy of any haemolytic streptococcal infections that may occur in rheumatic or non-rheumatic fever subjects.

(2) By contrast few advances have been made in the treatment of actual attacks of rheumatic fever. The early hope that corticosteroid therapy could control rheumatic carditis has not been borne out, and it may do harm if long continued. Salicylates are equally effective in the control of polyarthritis and fever, and may, like corticosteroids, be of some value in suppressing acute inflammation early in carditis.

(3) In the treatment of rheumatic fever, prompt and intensive penicillin therapy should be given for at least 10 days, along with either salicylates or steroids, in order to eliminate haemolytic streptococci which may still be active in the tissues.

If carditis is not evident, salicylates should be used

in preference to steroids. If carditis is evident, and treatment can be started within the first 3 weeks, most physicians favour prednisone 10 mgm. 4 times daily by mouth for 10 days, and thereafter reducing the total daily dose by 2–5 mgm. each day until therapy is discontinued. At present it is also suggested empirically that aspirin at the rate of 900 mgm. 5 to 6 times daily for adults should be given along with steroids, and thereafter continued as long as symptoms, fever, erythrocyte sedimentation rate, and C-reactive protein tests suggest continuing acitvity.

Complete bed rest should be continued only for the period of acute symptoms, and thereafter the patient should be allowed to sit up, and then to begin graduated walking exercise, so long as carditis is not present.

After the acute stage continuous prophylaxis with penicillin should be maintained indefinitely. Patients with inactive heart disease and without cardiac insufficiency should not have their physical activities limited.

It is emphasized that whereas the recommendations on prophylaxis can be made with assurance, those on therapy are still unproved, and are merely the best that can be made in the light of current knowledge.

H. Stanley Banks

GOLDBERGER, E. **The Etiology and Pathogenesis of Rheumatic Fever.** *Acta. Med. Scandinavica.* 1958, July, v. 161, No. 5, 347–59. [55 refs.]

"The concept has been presented that rheumatic fever develops as a result of two simultaneous processes: 1) a reinfection with a group A streptococcus of the same serological type which previously had caused infection; and 2) a specific antigen-antibody reaction, similar to, but not identical with serum sickness, which results from the reliberation of type-specific streptococcal M protein, into the systemic circulation.

"On the basis of this concept, prevention of rheumatic fever becomes a problem of preventing group A streptococcal reinfection. Prophylaxis with penicillin is effective in most patients. However, it has been suggested that groups of patients with a history of rheumatic fever should not be hospitalized or confined together, if possible because rheumatic fever represents a reinvasic type of communicable disease. In other words a patient can not only spread a streptococcal reinfection to other members of the group and so cause a reactivation of rheumatic fever, but can be similarly reinfected and similarly develop a reactivation of rheumatic fever, from any other member of the group.

"Similarly, the main object of therapy, once rheumatic fever develops, should be the elimination of group A streptococci from the body of the patient, in order to convert rheumatic fever into a self-limiting disease like serum sickness. Although penicillin theoretically is the drug of choice, it apparently is not able to kill streptococci, otherwise sensitive, which are in a state of low-grade metabolic activity. Methods of overcoming this difficulty, such as the concomitant use of streptomycin, and the concomitant use of cortisone or its derivatives, to reactivate metabolically the streptococci have been described."

Heart Disease

WORLD HEALTH ORGANIZATION. TECHNICAL REPORT SER. NO. 168. **Hypertension and Coronary Heart Disease: Classification and Criteria for Epidemiological Studies. First Report of the Expert Committee on Cardiovascular Diseases and Hypertension, Geneva, 13–18 October 1958.** 28 pp. [Refs. in footnotes.] 1959. Geneva: Palais des Nations. [Sales agent for U.K., H.M. Stationery Office.] [1s. 9d.; $0.30; Sw.fr. 1.–.]

This is a most useful report by the World Health Organization Expert Committee on Cardiovascular Diseases and Hypertension. After reviewing the present position in regard to the prevention and control of the various types of heart disease, they concluded that hypertension and coronary heart disease was the area in which knowledge about aetiology was least and the need for public health action greatest. Effective prevention will demand far more knowledge than is at present available about the distribution of the degenerative forms of heart disease in different population groups; and an epidemiological approach to the study of causes implies that comparisons, *e.g.* between populations in different countries, are based on clinical assessments made in some clearly specified standard fashion. Much of the report is therefore given over to laying down criteria of disease which might command wide acceptance and be useful in the conduct of comparative field studies.

The 4 main types of clinical manifestation of coronary artery disease are discussed: angina pectoris, myocardial infarction, sudden death and cardiac failure (mainly congestive in type). Definitions of "definite" and "probable" angina of effort are given and the differential diagnosis of the condition in field studies is discussed. The other conditions listed above are then dealt with in the same way. Perhaps the most useful part of the report, however, is the detailed description of electrocardiographic criteria for the diagnosis of coronary heart disease. Whether these will prove universally acceptable or not, they should form a most useful framework in the design of comparative field enquiries. The measurement of blood pressure is treated in some detail and arbitrary levels at which essential hypertension may be considered to exist are set out.

After reviewing the present state of knowledge about

aetiological factors such as diet, physical activity and smoking, the Expert Committee made a strong recommendation about the need to establish the true frequency of coronary heart disease, hypertension and related conditions in countries at different stages of development. To do the surveys required will need more cardiologists with training in epidemiology; and the Committee emphasized the urgency of providing training in this field. *D. D. Reid*

See also p. 1124, MORTENSEN, *et al.*, **Mortality due to Coronary Disease analyzed by Broad Occupational Groups.**

Cancer

BOUCOT, Katharine R., HORIE, U. & SOKOLOFF, M. J. **Lung Cancer detected by Survey Methods.** *Amer. J. Pub. Health.* 1959, June, v. 49, No. 6, 793–9, 7 figs.

The low 5-year survival rate for lung cancer does not necessarily mean that lung cancer does not go through a curable phase; it may mean only that it has not yet been possible to recognize this phase clinically. "Early" lung cancer might perhaps be defined as that stage of the disease which shows an abnormality in a chest X-ray, "within one year of a film which is still considered negative on retrospective review, even when the site of the subsequent cancer has been pointed out". So far, among 250 consecutive proved cases of lung cancer found by 2 chest survey units, only 19 fitted the definition and this number is too small for useful analysis. More such cases would be obtained, however, if physicians were persuaded to refer older men for 6-monthly X-rays.

The prognosis for patients who are asymptomatic at the time of the first abnormal film is substantially better than for those with symptoms, and very much better than for those in whom the disease is already clinically manifest; in the survey material the proportions alive after 3 years in the 3 groups have been 58%, 23% and 9% respectively. The prognosis was also found to be better in those in whom the first film was erroneously considered negative (52% alive in 3 years) than in those in whom the diagnosis was made radiographically (8%). It is, therefore, important that radiologists should regard any abnormality in the chest film as potentially indicating a neoplasm until the diagnosis is disproved.

It is recommended that (1) men over the age of 45 years should have 6-monthly chest X-rays, (2) symptomatic patients should be re-examined before being classified as "negative", (3) the highest standards of radiographic technique should be required, (4) readers of films should be kept alert by the inclusion of randomly allocated abnormal film, (5) Commissions should review the reasons for medical delay in individual cases, and (6) publicity should be given to the need for urgent medical attention when older persons develop symptoms. *Richard Doll*

JOULES, H. **Cigarette Smoking and Lung Disease.** *Trans. Ass. Indust. Med. Officers.* 1959, Apr., v. 9, No. 1, 9–13, 5 figs. [12 refs.]

Lung cancer mortality has increased out of all proportion in comparison with other cancers and we must regard ourselves as having to deal with an epidemic of cancer. That there is an association between lung cancer and cigarette smoking has been agreed by all the independent bodies which have been set up to examine the evidence. Objections to the conclusion that cigarette smoking is a cause of the disease have been raised on the grounds that animal experiments have failed to substantiate the findings and that there is no connexion between cigarette consumption and changes in the bronchial mucosa. The latter is no longer tenable as AUERBACH and his colleagues [this *Bulletin*, 1957, v. 32, 448] have demonstrated that with smoking there is a gradual mucosal change leading through hyperplasia and metaplasia to carcinoma-in-situ.

Data for the U.K. show a rise in tobacco consumption between 1881 and 1955, and a very great rise in the consumption of cigarettes since the beginning of the century. Women, however, have smoked cigarettes in quantity only since 1940 and this lag in consumption may go far to explain the present sex incidence of the disease (now 7 : 1). Prospective studies of the mortality among men with different smoking habits have shown that cigarette smoking is more conducive to lung cancer than pipe or cigar smoking and that the mortality from the disease becomes progressively lower as the length of time increases after regular smoking has stopped.

Chronic bronchitis is probably commoner in Britain than anywhere else in the world. It accounts for 10% of all time lost due to illness in industry. A much higher proportion of the sufferers are heavy cigarette smokers than of those of similar ages in the general population. Atmospheric pollution, dust and fumes at work, and infections appear to act synergically with cigarette smoke to produce the disease.

The facts should be constantly publicized; if doctors, nurses and health visitors cannot give up smoking, they should smoke only in private. The significance of vested interests must also be recognized if we are not

to enter the second industrial revolution burdened by a legacy of preventable chest disease. *Richard Doll*

BURGAN, J. G. **The Manufacturers' Contribution to Experimental Research on Smoking and Lung Cancer.** *Trans. Ass. Indust. Med. Officers.* 1959, Apr., v. 9, No. 1, 13–17, 3 figs.

Progress in the experimental investigation of smoking and lung cancer depends on developing a realistic means of testing tobacco smoke biologically. The manufacturers have not felt qualified to carry out this type of research but their knowledge of the chemistry of tobacco smoke may enable them to make a real contribution in other ways. For example, they have worked on:

1. Problems in the basic physics and chemistry of smoke. It has been demonstrated that the chemical constitution of tobacco smoke is appreciably affected by the conditions under which the cigarette is smoked. Machines which obtain a constant volume of smoke at each puff and others which draw the smoke at a constant pressure have been used to show the effects of varying the volume, duration and frequency of the puff. For example, puffs of 35 ml. volume and 2 seconds' duration, drawn at 1 per minute, lead to a lower ratio of volatile to total nitrogen in the smoke and a higher ratio of total acids to total nitrogen, than puffs of 15 ml. volume and 2 seconds' duration, drawn at 4 per minute. Smoke composition is also affected considerably by the type of leaf. 3 main types are used. Air-cured tobacco is the natural end product when green leaf is allowed to respire naturally till it dies; it is characterized by the absence of carbohydrate and is an important constituent of American cigarettes and of many pipe mixtures. Other leaves are fermented, and changes occur in the protein and alkaloid content; these are used for cigars in the U.K., and for cigarettes in Russia and Central Europe. In flue-cured tobacco, respiration of the leaf is stopped by heat and the tobacco contains reducing sugars. It is used for British cigarettes. The smoke from these 3 types contains different proportions of total nitrogen, volatile nitrogen, acid etc., and this may be significant in view of the different amounts of lung cancer reported in different countries and the different methods of smoking.

2. Investigation of specific constituents of tobacco smoke. Special attention has been paid to 3 : 4-benzpyrene, as it is thought to be a useful model substance. The leaf, before smoking, contains approximately 10 μgm. per kgm. as a result of contamination in the process of preparation. During smoking most of this is destroyed, but more is formed and the smoke finally contains about the same quantity. 2 compounds —copper nitrate and platinum diamminonitrite—reduce the content of benzpyrene in cigarette smoke by up to 80%.

3. Problems in the large scale preparations of smoke condensates. Each cigarette must be smoked individually and a method has been evolved by which the condensable material is collected quickly after leaving the cigarette in a trap cooled to around $-70°C$. Standardized smoke condensate, prepared in this way, has been provided for research workers, so that experiments can be carried out with uniform material and the results made more readily comparable. *Richard Doll*

BASTAI, P. & PESCETTI, G. **Aetiological Factors of Bronchogenic Carcinoma.** *Panminerva Med.* Turin. 1959, May, v. 1, No. 1, 6–10. [Numerous refs.] [Abridged translation from *Minerva Med.* 1959, v. 50, 1.]

The possible aetiological factors are reviewed against the background of the known great increase in the incidence of the disease. It is concluded that the 2 main factors to be considered are tobacco smoke and atmospheric pollution. Their relative importance is illustrated by 2 recent observations. First, WYNDER and LEMON [no reference given] showed that the disease was very rare among "Adventists" who, because of their religion, do not smoke or drink. Many, however, live in industrial towns in the U.S.A. and are exposed to pollution in the same way as the general population. Secondly, the mortality from tumours of the respiratory tract in Venice is one of the highest to be recorded in any part of Italy and is higher than that in the industrial centres of Milan and Turin. The consumption of tobacco in the Venice region is "not significantly different from that of other cities in north Italy", but the degree of atmospheric pollution must be much less because the island contains no factories and road traffic does not exist. In the authors' opinion these facts, taken in conjunction with other evidence, provide "the most convincing proof that tobacco smoke is the main cause of the increased incidence of bronchogenic carcinoma". *Richard Doll*

AGNESE, G. Sui rapporti fra consumo di tabacco e mortalità per tumori maligni del polmone in Italia. **[The Relationship between Tobacco Smoking and Mortality Rate for Lung Cancer in Italy]** *Igiene Moderna.* 1958, Nov.–Dec., v. 51, Nos. 11/12, 801–20, 3 graphs. [17 refs.] English summary.

Study of the available data for 19 Italian regions shows that there is a strong correlation between lung cancer mortality in 1952–4 (standardized for the proportion of the population aged 45 years and over) and the consumption of tobacco per head of the population aged 18 years and over. The extent of the correlation varies with the type of tobacco; it is strongest for cigarette consumption ($r = 0{\cdot}887$), is very much smaller for cigars ($r = 0{\cdot}263$) and is negative for pipe tobacco ($r = 0{\cdot}193$). The small positive correlation with cigar consumption, moreover, disappears when the consumption of cigarettes is held constant. The data are not available for the different types of tobacco in smaller units, but data for total tobacco consumption for the longer period 1927–54 for 91 provinces show a correlation similar to that for the 19 regions.

Similar results are obtained when the lung cancer mortality at a given period is compared with the tobacco consumption of an earlier period. National data for the whole of Italy show that lung cancer mortality has increased while cigar and pipe tobacco

consumption have been decreasing. Cigarette consumption, however, has increased sharply and the correlation between lung cancer mortality and the consumption of cigarettes 20 years previously—chosen to allow for a prolonged latent period—is close (r = 0·883).

Richard Doll

AGNESE, G. Sui rapporti fra mortalità per tumori maligni del polmone in Italia ed alcuni sospetti fattori favorenti. [**Relationship Between Lung Cancer and Suspected Favouring Factors in Italy**] *Igiene Moderna.* 1958, Nov.–Dec., v. 51, Nos. 11/12, 821–44. [14 refs.] English summary.

Data available for 19 Italian regions enable an examination to be made of the correlation between the mortality from lung cancer during the period 1952–4 and the prevalence of the various factors which contribute to atmospheric pollution. In the calculations, lung cancer mortality is corrected for the proportion of the population aged 45 years and over, cigarette consumption is related to the population aged 18 years and over, the intensity of motor traffic is measured by the number of licensed vehicles per km. of road (other possible indices of motor traffic show lower correlations), industrialization is measured by the proportion of inhabitants aged 11 years and over employed in industry and the average winter temperature is used as an index of domestic fuel consumption. The correlations between lung cancer mortality and (1) cigarette consumption and (2) motor traffic are highly significant. The former remains significant when the index of motor traffic is held constant (r = 0·707) and when both the other factors are also held constant (r = 0·547); the first order partial correlation coefficient for lung cancer mortality and motor traffic with cigarette consumption constant is, however, not significant.

The data for lung cancer mortality and cigarette consumption were also examined in relation to the mortality from other malignant tumours, the mortality from bronchitis, and population density (used as a simple index of general hygiene and socio-economic factors). In this instance, substantial correlation was also found between lung cancer mortality and mortality from other tumours, but this was largely accounted for by the correlation between other tumour mortality and the consumption of cigarettes.

Finally, a comparison was made between lung cancer mortality in the 91 Italian provinces in 1953–4, the annual consumption of cigarettes per head, the two other factors which appeared likely to have any significance in the previous study (the index of motor traffic and the mortality from other tumours) and a more specific index of industrial activity, *i.e.* the proportion of inhabitants employed in the metallurgical, engineering and chemical industries. Once again the first order partial correlations between lung cancer mortality and cigarette consumption are highly significant but in this instance the correlations with motor traffic and specific industrialization with cigarette consumption held constant, are also significant—though less highly so.

Examination of data for 9 Italian cities shows that high lung cancer mortality can be present in the absence of motor traffic and of industrialization and it is concluded that the consumption of cigarettes is the outstanding factor of importance. *Richard Doll*

LAWTHER, P. J. & WALLER, R. E. **Atmospheric Pollution and Lung Cancer.** *Trans. Ass. Indust. Med. Officers.* 1959, Apr., v. 9, No. 1, 5–8, 1 fig. [19 refs.]

2 good reasons for suspecting that air pollution may cause lung cancer are: (1) that urban air contains substances known to be carcinogenic, and (2) that the disease occurs more often in towns than in the country. The substances in the air include 3 : 4-benzpyrene, 1 : 2-benzanthracene, 1 : 12-benzperylene, benzene, chrysene, epoxides and arsenic; doubtless others await identification. Special attention has been paid to 3 : 4-benzpyrene, but extrapolation from animals is dangerous and it cannot be assumed that it necessarily causes lung cancer in man. It is difficult also to make simple quantitive estimates of the physiological effects of different atmospheres, because variations in the particle size of the smoke and the degree of particulate aggregation will have important effects on the proportions of substances retained at different sites in the respiratory tract.

STOCKS (*Brit. J. Cancer*, 1952, v. 6, 99) has demonstrated that in England and Wales the mortality from lung cancer is higher in large than in small towns and that within London it is higher in the more densely populated and heavily polluted areas north and east of the city. Concentrations of smoke and of polycyclic hydrocarbons are higher in large towns, but other factors may also be associated with high population density. KREYBERG, [this *Bulletin*, 1957, v. 32, 579] for example, found a high urban : rural ratio of mortality in Norway, despite a very low level of pollution. Smoking habits must be taken into account and they might be of special significance, if the change in habit from pipe to cigarette smoking spread from the large towns to the rural areas between 20 and 40 years ago. There is, however, direct evidence that living in large towns can provide an additional risk of lung cancer for non-smokers [HAMMOND and HORN, *ibid.*, 1958, v. 33, 753].

It is reasonable to infer that air pollution plays some part in the causation of lung cancer, but not that it is the cause of the rise in the incidence of the disease. It is, indeed, probable that city air has become cleaner, because of the increased use of gas, electricity, oil and coke. The diesel engine is a new source of pollution, but it has not been used long enough to have been responsible for the increased incidence of the disease. 3 : 4-benzpyrene has been found in the smoke produced by an inefficiently operated diesel engine and also in the exhaust from petrol engines, but there is little evidence that either source adds a substantial amount of carcinogenic material to the air which is actually inhaled. Investigation of the air pollution in London Transport bus garages showed that on a winter's night the concentration of 3 : 4-benzpyrene was much the same inside as out; on a fine clear night in early summer it was found that the buses could be adding some benzpyrene, but less than one-tenth of that found in the outside air in winter. Study of London Transport

staff has, however, failed to show any excess incidence of lung cancer, such as would be expected if diesel exhaust fumes were a serious contributory factor.

Richard Doll

BORNEFF, J. & KNERR. R. Cancerogene Substanzen in Wasser und Boden. I. Theoretische Grundlagen, Eigenschaften und Nachweis. [**Carcinogenic Substances in Water and Soil. I. Theoretical Basis, the Nature of the Substances and their Recognition**] *Arch. f. Hyg. u. Bakt.* 1959, Aug., v. 143, No. 5, 390–404, 5 figs. [Numerous refs.]

In this long paper the authors in their introduction write of the possible dangers to the public of water which has become polluted by carcinogenic substances derived from a variety of industrial wastes which may be present in traces in the atmosphere. Tar and mineral oil may also contain carcinogenic substances as well as acting as solvents for these. Detergents also may be dangerous to health.

A classified list of the most important carcinogenic agents is given with details of their chemical nature and physical properties. Finally there is a description of the scientific bases of spectrophotometric and chromatographic methods for the qualitative and quantitative analysis of 3 : 4-benzpyrene and 1, 2, 5, 6-dibenzanthracene. The results obtained with these methods are to be published later. *M. E. Delafield*

Dental Hygiene

AUSTRALIAN DENTAL J. 1958, v. 3, Nos. 5 & 6, 309–30; 378–98, 12 figs. [Numerous refs.] **The Biology of the Children of Hopewood House, Bowral, N.S.W. II. Observations extending over Five Years (1952–1956 Inclusive).**

Hopewood House and its annexes in other parts of New South Wales are controlled by the Youth Welfare Association of Australia. The dietary of the children is notable for its complete lack of meat and refined sugar. Vegetables, mostly raw, constitute the major part of the meals, while "a well-equipped dairy provides all the milk and cream required, but such items as eggs and butter are purchased regularly from the town. Whole-meal bread and, to a lesser extent, white bread are obtained from a local bakery".

There is no organized tooth-brushing by the children, and their oral hygiene is unsatisfactory, but their caries experience is remarkably low. For example, at the age of 13 years, the average DMF (decayed, missing, filled) figure for Hopewood children was found to be 1·06, while the corresponding figure for the average child of the same age attending State schools in N.S.W. was 10·70. The percentage of Hopewood children, aged 13 years, having caries-free permanent teeth was 53·1; for State schoolchildren of the same age it was 0·4.

Accounts are given of the:—

Lactobacillus counts of the Hopewood children,
Dietary surveys at Hopewood House,
Physical health of the Hopewood children,
Occlusal condition of the Hopewood children.

[The number of children surveyed in this investigation was 82, which is too small a figure to enable firm conclusions to be drawn regarding the effect of the children's dietary.] *Robert Weaver*

Occupational Hygiene

In this section the abstracts are arranged as far as possible in the following order: General; Mining and Dust Diseases; Poisoning due to Metals, Solvents and Other Substances; Skin and Other Affections; Radio-Active Substances; Other Conditions; Occupational Psychology

BISHOP, W. H. H. **A Three-Year Report on Morbidity in Some Ontario Industries.** *Canadian J. Pub. Health.* 1959, Apr., v. 50, No. 4, 152–8.

In this report from the Division of Industrial Hygiene, Ontario Department of Health, sickness absence data from 1955 to 1957 have been collated from returns made by Ontario companies engaged in various industries, employing between 250 and 1,700 workers. The returns were of 2 different kinds. 8 companies reported absences from work due to sickness and accidents, 9 companies reported conditions leading the employee to seek advice at the company's health centre; 3 of these companies rendered both kinds of return. In a uniform system, designed by the Ontario Department of Health, disease was classified in 19 diagnostic groups, by using the section headings of the 1948 revision of the International list [this *Bulletin*, 1949, v. 24, 720]. 2 fre-

quency rates were used, both derived from average figures for the 3-year period: the absence rate, *i.e.* the average number of morbidity absences per 100 employees; and the reporting rate, *i.e.* the average number of new conditions of morbidity reported to the health centre per 100 employees.

30·3% of all absences from work were due to acute upper respiratory infections, and the next commonest causes of absence were successively diseases of the digestive system, other respiratory diseases, and symptoms and ill-defined conditions. Accidents only accounted for 5·1% of absences from work. The total frequency rate for all diagnostic groups was 134 absences per 100 employees per year.

The most frequent causes of employees seeking advice from their company's health centre were accidents and violence, comprising 40% of all conditions. The next 3 most frequent causes were, successively, acute upper respiratory infections, symptoms and ill-defined conditions, and diseases of the digestive system. The total reporting rate for all diagnostic groups was 582 new conditions per 100 employees per year.

In the case of the 3 companies which reported both absence from work and health centre attendance according to the same diagnostic groups, it was possible to make a direct comparison between the two indices. For instance, diseases of the skin and cellular tissue caused attendance at the health centre 12 times as frequently as absence from work. Accidents and violence, similarly, caused 22 times as many health centre attendances as absences. The author suggests that in these cases utilization of the health centres may have reduced the number of absences from work. *A. S. Fairbairn*

PARMA, C. Berufsschäden der Zahnärzte. [**Occupational Disorders of Dentists**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1959, May–June, v. 5, No. 3, 152–75, 2 figs.

This is an extremely detailed paper in which there is an analysis of information obtained by questionnaire and by sickness reports on the illnesses and disabilities suffered by members of the dental profession in Czechoslovakia. The questionnaire was answered by 2,785 persons (2,302 men and 483 women) who worked in the cities and provinces of the republic. The data collected are set out in 12 tables with a wealth of clinical detail. The prevalence of the different types of illness in dentists is compared with that recorded in other occupations. There is much description of the results of the study and some discussion of preventive measures.

The conditions which as a result of this work are considered to be occupational diseases of dentists are: (1) teno-synovitis, neuritis and arthritis of the upper extremity, (2) eczema and dermatitis of the hands, (3) infections resulting from increased risk of droplet infection such as inflammations of the upper respiratory passages and the eyes and also some general infections such as diphtheria and scarlet fever, and (4) accidents involving the hand and the eye. Conditions which are brought to light or made worse by dental work are: (1) flat feet, (2) varicose veins, (3) kyphoscoliosis and (4) spondylitis. *M. E. Delafield*

MORTENSEN, J. M., STEVENSON, T. T. & WHITNEY, L. H. **Mortality due to Coronary Disease analyzed by Broad Occupational Groups.** *Arch. Indust. Health.* Chicago. 1959, Jan., v. 19, No. 1, 1–4, 3 charts.

The authors have investigated the mortality in 1951–5 from coronary disease and other causes among male employees aged 40–64 of the Bell Telephone Companies in the United States. Death rates in 3 managerial grades (officials, supervisors and staff, and foremen) and 2 non-managerial grades (craftsmen and labourers, and clerks) were calculated from a total of 1,082 deaths and 375,000 man-years of exposure.

Mortality is expressed as a ratio of actual to expected deaths. [Presumably the expectation is derived from different age-specific rates within the age group 45–64 for all employees, though this is not clearly stated.] There was a significant difference between this ratio in the management group, 106%, and that in the non-management group, 96%. The "top management", however, showed the lowest coronary mortality of all groups of employees. A high death rate from coronary disease in clerical employees was thought to be due to a transfer into this group of physically impaired craftsmen. The management group had a higher mortality from coronary disease than the non-management group in every 5-year age-group from 40 to 64, except at ages 50–54. A strikingly high managerial mortality at 60–64, could be due to differential retention of impaired men in these grades. Coronary mortality among all active employees (not coded occupationally) was also compared at different ages with that of service pensioners. The relatively high rates for service pensioners before 65 show the high proportion of impaired lives in the retired group. The combined death rates from coronary disease of active employees and pensioners, however, showed little difference from those of active employees alone, owing to the small numbers of employees who retired before the age of 65. Both these rates are just a little lower in each age-group than the corresponding rates for the general male population of the United States.

The authors conclude that there is a marked difference in coronary mortality between "top management" and "middle management" which cannot be explained from the available data. "Top management" had the lowest mortality of all groups and the popular notion that high executive positions carry a risk of high mortality from coronary disease may be due to the greater publicity connected with such deaths.

A. S. Fairbairn

FERNÁNDEZ ROZAS, F. El control tecnico ambiental acoustico en las sorderas profesionales. Estudio médico legal: Su valoración conforme a la ley No. 9688 y su decreto reglamentario. [**Technica' Control of Noise in relation to Occupational Deafness. A Medico-Legal Study. Assessments under the Act No. 9688 (Workers' Compensation) and the Regulations made thereunder**] *Semana Méd.* 1959, Apr. 16, v. 114, No. 16, 497–503.

In the Argentine Republic compensation is payable to those afflicted with occupational deafness. It is based

on previous earnings and is expressed as a percentage of them.

In the examination of claims it is necessary to inspect the place of work and measure the intensity and type of noise.

In examining claims a history of previous occupations must be obtained: the hearing tested and an audiogram taken: a clinical examination made and a general medical history taken: the acoustic history should indicate whether or not the hearing loss is constant and, if not, what makes it worse. It must be determined whether the patients' work has caused, or only aggravated, his deafness, whether he is deaf in one or both ears and whether or not there is any vertigo, all of which affect the amount of his compensation. Sometimes the deafness is due to cerebral trauma when there may also be ocular lesions.

The basic scale of compensation is set out. When he can hear a whisper at a distance of 0·25 to 0·5 cm. and the ordinary speaking voice at 4 to 5 metres it is 5 to 8% for unilateral and 15 to 20% for bilateral deafness: it is 45% when it is bilateral and he cannot hear even a shout: in severe deafness accompanied by serious vertigo it is 50 to 70%. *Allen Daley*

KATHREN, R. L., PRICE, H. & ROGERS, J. C. **Air-Borne Castor-Bean Pomace Allergy.** *Arch. Indust. Health.* Chicago. 1959, May, v. 19, No. 5, 487–9.

Castor oil pomace is the solid residue remaining after the oil is extracted from the beans. It is a source of nitrogen used in fertilizers and is well-known to contain substances, not present in the oil, likely to produce allergic symptoms such as rhinitis, asthma, dermatitis and conjunctivitis.

4 men working in a pipe reconditioning company 250 years down wind of a fertilizer plant complained of sudden and severe attacks of asthma. On investigation the attacks were found to coincide with a dusty operation involving mixing and sacking solvent-extracted desiccated pomace. When the firm changed over to an oily pomace remaining after oil had been extracted by crushing and pressing beans, the allergic attacks in the pipe company workers ceased.

T. O. Garland

PESTALOZZI, C. Febrile Gruppenerkrankungen in einer Modellschreinerei durch Inhalation von mit Schimmelpilzen kontaminiertem Befeuchterwasser ("Befeuchterfieber"). [**Febrile Disease in Carpenters in a Carpentry Works through Inhalation of Moist Air Contaminated by Moulds**] *Schweiz. med. Woch.* 1959, July 4, v. 89, No. 27, 710–13. [12 refs.]

This paper contains an account of the investigation of a mysterious illness which was affecting, with increasing frequency, the workers in the carpentry workshop of a large machine factory. The chief symptoms and signs of the illness were extreme lassitude with cough and breathlessness and at night high fever, rigors and profuse sweating. By next day the patients were usually well enough to resume work. This condition occurred most frequently on Mondays but never during holidays. The work was carried out in a large, airy workroom the atmosphere of which was kept moist by an aerosol apparatus which is described.

Some details are given of the investigations carried out at the Dermatological Clinic of Zürich University. Scratch tests on the workers with dusts from the workroom and with an *Aspergillus* strain were negative but mycological examination of the water from the humidifier showed the presence of various kinds of *Penicillium, Aspergillus, Mucor, Scopulariopsis, Cephalosporium* and *Trichoderma.* At a later date 14 of the workers were given an intradermal inoculation of a mixed extract of these moulds with the result that although there was no immediate skin reaction most of the workers suffered from the typical symptoms of the general illness. When the aerosol apparatus was adequately cleaned and sterilized no further cases of this illness occurred. The similarity of this disease (which is here called *Befeuchterfieber*) to threshers' disease and others which are considered to be caused by allergic reaction to moulds is discussed. *M. E. Delafield*

UYTERLINDE, B. De boerenlong, een acute longziekte na het dorsen van beschimmeld graan. ["**Farmer's Lung", an Acute Pulmonary Disease due to Threshing Mouldy Grain**] *Nederl. Tijdschr. v. Geneesk.* 1959, Feb. 28, v. 103, No. 9, 457–9, 1 fig. [10 refs.] English summary (6 lines).

A case of acute farmer's lung is described. The patient was an agricultural worker aged 66 who was admitted to hospital in Rotterdam in October 1957 with pyrexia of unknown origin of 16 days duration. The onset was acute, with rigors and pyrexia to 40°C., and took place 3 days after the patient had threshed mouldy corn in a barn, a procedure which produced so much dust that visibility was reduced to a few inches. There was some dyspnoea and a slight cough, and auscultation of the chest revealed vesicular breathing. X-ray examination showed many small opaque areas scattered over both lung fields. There was no sputum. *Candida albicans* and *C. pseudotropicalis* were isolated from the stomach contents. The patient was given 1 gm. of potassium iodide 3 times daily and the temperature returned to normal. On out-patient examination after 2 months the patient was symptom-free and had regained full working capacity. *D. J. Bauer*

FREYTAG, J., NICEWICZ, W. & PLESZCZYNSKI, W. Untersuchungen über die Staubverdichtung beim Dreschen mit fleichzeitiger Bestimmung der Mikroflora des Staubes. [**Dust Concentration during Threshing Work and Investigation of the Microflora of the Dust**] *Arch. f. Hyg. u. Bakt.* 1959, Aug., v. 143, No. 5, 321–33. 12 figs. [50 refs.]

In a large number of agricultural activities such as threshing, harrowing, seed sowing, application of chemical fertilizers and the preparation of animal foodstuffs, the workers are often exposed to heavy concentrations of dust in the atmosphere. In this paper the authors consider particularly the dust which arises during threshing. Some of the literature on the inorganic and organic constituents of threshing dusts, the sizes of

the dust particles and their concentration in the atmosphere is described.

In the medical examination of 7 women (aged 17–22 years) and 4 men (aged 20–22 years) who were exposed to threshing dusts in their work, it was found that all suffered from marked catarrh of respiratory mucous membranes with muco-purulent discharge. The symptoms were cough, pains in the chest, some difficulty in breathing, noises in the ears, a burning feeling in the eyes and loss of appetite.

Most of the paper is devoted to a description of the results of mycological examination of the dusts and of swabs from nose and throat of the workers. There is a classification of the isolated organisms and a few photographs. A total of 139 strains belonging to 22 genera of the "fungi imperfecti" group were isolated.

M. E. Delafield

LIDDELL, F. D. K. & MAY, Joan. **A Statistical Study of Coal-Mining Accidents.** *Brit. J. Indust. Med.* 1958, Oct., v. 15, No. 4, 262–9, 1 fig.

3 sources of data were used in this study. (a) A sample of returns made to the British National Coal Board between 1945 and 1949 of all compensatable casualties, from which a "casualty rate" was calculated, *i.e.* the number of casualties in a class of worker divided by the number of workers in that class. (b) A more detailed investigation made at 14 collieries, in 2 different areas, of all compensatable casualties. (c) "Accident rates", *i.e.* the number of accidents divided by the number of man-shifts in the year; these were calculated for every colliery in the United Kingdom in 1953 and 1954. These were related to various characteristics of the colliery, *i.e.* the "colliery profile".

Fatal casualty rates were highly correlated in the various divisions of the Coal Board with the rates for other serious casualties which were reportable to the Mines Inspectorate. No such correlation, however, was found between the frequency of these serious casualties and that of the less serious compensatable injuries. These rates, unlike those of the more serious casualties, were probably affected by different standards of reporting in different areas. Furthermore, the frequency of serious injury has been steadily decreasing since 1927, while other compensatable accidents showed a sharp increase in 1948, when the National Insurance (Industrial Injuries) Act came into force.

There was a consistent gradient in the casualty rates from those of coalface workers, which were highest, through those of other underground workers to the rates for surface workers, which were lowest. The data for the 3 classes of worker have therefore been analysed separately. The casualty rates in each class show a steady decrease with age, while the length of absence tends to increase with age. There is, however, little difference with age in the rates of the more serious injuries. A combined analysis by age and severity of injury, within each class of worker, showed that when account was taken of the severity of injury, there was little difference in the length of absence with age.

It was found from the more detailed analysis of data (b) that no single occupation within any of the 3 classes had consistently high or consistently low casualty rates. Men in different occupations tended to suffer from different types of injury, but this pattern itself varied from pit to pit.

Coal-face workers suffered 6·8 times as many slight injuries as serious ones. This ratio was only 3·5 for surface workers. These ratios, however, tend to obscure the fact that coal-face workers still suffer twice as many serious injuries as do surface-workers.

There was no indication that the underground accident rate or the surface accident rate increased with the size of the colliery. The relationship of the accident rate to the size of mine, previously reported by the Acton Society Trust (1953, *Size and Morale*, London) and by others, may have been due to the higher likelihood of accidents in pits with shafts, which predominate among the larger mines. On the other hand it was found that there is a strong tendency for collieries with high underground accident rates to have high surface accident rates as well. There was also an association between the accident rates of collieries in each of the 2 consecutive years 1953 and 1954.

No relationship was found between the frequency of accidents and a number of other factors derived from both data (a) and data (b). This reflected in the authors' opinion the poor quality of the data, which were collected for purposes other than research. It could not be inferred that these factors were of no importance.

A. S. Fairbairn

MINISTRY OF LABOUR & NATIONAL SERVICE. **Industrial Health. A Survey of the Pottery Industry in Stoke-on-Trent. A Report by H.M. Factory Inspectorate.** pp. v + 78. 1959. London: H.M. Stationery Office. [5s.]

This is a Report on an Industrial Health Survey of the Pottery Industry in the Stoke-on-Tent area which was carried out from 1956 to 1958 by 4 members of H.M. Factory Inspectorate. The survey was undertaken with the advice of the Industrial Health Advisory Committee of the Ministry of Labour and National Service. The aim was to present an objective detailed and informed picture of existing conditions in the industry and to indicate outstanding problems. Altogether 298 factories—virtually all the pottery works in North Staffordshire—were visited. This represents approximately 63% of the pottery works in the country and approximately 75% of the workers in the industry.

In 1956 the pottery industry in North Staffordshire employed 48,184 persons in 298 factories of which 63 had more than 250 workers; 2 factories only employed more than 1,000 workers. Approximately 60% of the employees were women. In the decorating departments, of the 10,643 persons employed 9,819 (92%) were females. The inspectors found that nearly one-half of all the factories had undergone no significant reconstruction since 1938 and that modern factories were extremely few. There had, however, been a considerable diminution in bottle ovens owing to the development of gas and electrically fired tunnel ovens.

The Report examines in detail the various processes of pottery manufacture and their attendant health hazards. Pneumoconiosis is still the most important specific health risk of potters. During the past 20

years the disease has been controlled in the china section by the replacement of flint by alumina. Lead poisoning, formerly a very serious hazard in the glazing processes, has been virtually eliminated by the prohibition of raw lead glazes in favour of leadless and low-solubility lead glazes. Dermatitis is a risk in some processes and ocassionally injury to health may arise from organic chemicals, hydrofluoric acid and other fluorine compounds, ceramic colours and carbon monoxide.

The environmental part of the survey revealed that the potters' shops were often excessively, sometimes illegally, hot, and at sóme points very dusty. Standards of general cleanliness, washing accommodation, sanitary accommodation, messrooms and first-aid boxes were often deficient, indeed in breach of regulations. Medical supervision of the health of the workers was almost entirely represented by the statutory duties of the Appointed Factory Doctors and the Pneumoconiosis panel.

[With regard to the stated aim of the survey one admits that the Report is objective; indeed it does not hide deficiencies in supervision by the Factory Inspectorate. The medical facts, however, are far from detailed.] *A. Meiklejohn*

McIntyre Research Foundation. **Ninth Conference on Silicosis and other Industrial Pulmonary Diseases held in Toronto, Ontario, Canada, January 27, 28 and 29th, 1958.** 12 papers, illustrated. [Numerous refs.] 1958 and 1959. Toronto 1: Suite 1500, 25, King Street West.

The pattern of the annual conference of the McIntyre Research Foundation on silicosis and kindred subjects is now well established [see this *Bulletin*, 1958, v. 33, 954 for review of eighth conference]. At this ninth conference there were 12 papers including the short opening address of the president, W. B. Dix. For the purpose of reviewing the papers it seems better to group them by affinity of subject-matter rather than to adhere strictly to the sequence of presentation.

Victoria M. Trasko. *Silicosis—A Continuing Problem.*

During the 19th century references to the occurrence of occupational diseases of the lungs in U.S.A. were sporadic. Present interest in the problem was initiated by F. L. Hoffman of the Prudential Life Insurance Company, who in 1907 and 1918 compiled statistics which revealed the excessive mortality from tuberculosis in dusty occupations. Miss Trasko has sought through various sources to discover the more recent prevalence and trends of silicosis in the United States. The results, which are the basis of the lecture, have already been published elsewhere [*ibid.*, 1959, v. 34, 236].

W. C. Wheeler and A. H. Sellers. *Some Observations on Silicosis Statistics in Ontario.*

At the Third Conference of the McIntyre Research Foundation in January 1951, the history and early development of a plan to produce statistics of silicosis in Ontario were outlined. Progress reports were presented at the Conferences in February 1954, and in October 1956 [*ibid.*, 1958, v. 33, 954]. The present paper brings these statistics up to date. The original purpose of this clinical statistical research was to assist in control of the disease. Trends, so far observed, in prevalence and severity of the disease are regarded as encouraging.

W. B. Ayre. *Silicosis in the Foundry—Medical Control.*

Silicosis became a compensatable disease in the Province of Quebec in 1942. Ayre, then medical officer at a large steel foundry, here records his experience of silicosis among various occupational groups from 1942 to 1957. The steady improvement reflects the value of environmental and medical control.

[See below p. 1132.]

R. E. Findlay. *Management's View on the Prevention of Silicosis.*

The definition of silicosis in the Workmen's Compensation Act, Ontario, is:

> "Silicosis shall mean the fibrotic condition of the lungs, sufficient to produce a lessened capacity for work, caused by the inhalation of silica dust."

The importance of silicosis to employers is proved by a study of compensation payments in respect of disablement and death by the disease. In Ontario the Mining Association have compiled records, including follow-up, of cases since 1926 and these are presented in a series of highly informative tables. Table 4 includes details of 759 deaths which occurred among silicotics between 1926 and 1957. The cause of death was attributed as follows: silicosis 18 (2·4%) cases; silicosis and tuberculosis 451 (59·4%); and other causes, 290 (38·2%).

[At a future conference of the Foundation more detailed information and comment should be made on the 290 cases attributed to other causes. One can accept that silicosis was not the proximate cause of death. In Great Britain the Pneumoconiosis Medical Panel in certifying whether or not death has been caused by pneumoconiosis must consider substantial aggravation and acceleration by the disease.]

J. V. Skendall. *The Study of the Claimant for Silicosis Compensation.*

This contribution was divided into 3 parts by separate authors.

Part I.

Skendall, Safety Director, Harbison-Walker Refractories Company, Pittsburg, Pa. dealt with the legal aspect.

There is no uniformity in the Workmen's Compensation laws in the United States. This applies to benefits and to criteria for existence of occupational diseases, and specifically for existence of silicosis. The following definition from the legislation in the State of Montana is of interest:

> Silicosis = "A fibrotic condition of the lungs due to the inhalation of silica dust which results in total disability to do manual labor."

Part II.

L. H. Osmond. *Some Considerations Concerning the Roentgen Diagnosis and Conditions that may simulate it.*

This is a comprehensive account of the radiographic diagnosis and differential diagnosis of silicosis. It is

noteworthy for a large series of well-reproduced radiographs.

Part III.

In this concluding part Dr. J. W. G. HANNON discusses the clinical aspects with special reference to diagnosis of the disease and assessment of resultant incapacity by measurements of pulmonary function.

P. C. KOECHEL. *The Industrial Relations Aspects of Aluminium Therapy.*

The Mesta Machine Company have been engaged since 1898 in the production and finishing of steel castings, ranging in size from 500 to over 700,000 lb. (approx. $\frac{1}{4}$–300 tons). Silicosis and tuberculosis appeared as risks among the workmen, particularly the chippers (fettlers). Every endeavour was made to diminish the creation of dust and to remove any dust which escaped, by appropriate ventilation methods. The workmen were encouraged to wear respirators and a programme of initial and periodical medical examination, including chest radiography, was established. These measures were only partially successful. In 1948 aluminium therapy was introduced and in 1954 for the first time not a single new case was discovered in the plant. The Company think that they have overcome the problem of silicosis and that aluminium therapy not only arrests silicosis but also prevents it.

[Mr. Koechel does not provide any scientific evidence in support of this opinion. It may not be without relevance to reprint clause 3 of the contract between the McIntyre Research Foundation (the licensor) and its users (licensees) of aluminium powder:

> 'It is the essence of this agreement that Licensee shall keep the dust on said premises to a minimum, for Licensor and Licensee agree that the said invention is not a substitute for dust preventative measures in combating silicosis hazards . . .".]

E. B. GILLANDERS. *The Industrial Hygiene Aspects of Uranium Mining in the Algoma District.*

The Rio Tinto Mining Company of Canada operates 4 uranium mines and surface plants in East Algoma, Ontario. The plants have an aggregate daily capacity of nearly 20,000 tons of ore. Underground workmen are exposed to radio-active and siliceous dusts and to diesel fumes, while surface plant operatives may suffer from the inhalation, ingestion or absorption through the broken skin of uranium oxide. This risk is controlled primarily by dust control, good housekeeping and personal cleanliness. The extent of body absorption of uranium is determined by urinalysis, with a maximum permissible concentration of 50 micrograms per litre.

The paper includes the text of the Code of Requirements for the Survey of Dust, Ventilation and Radioactivity at Uranium Mines in Ontario, as issued by Ontario Department of Mines.

L. A. CARAPELLA. *Radioisotopes in Industrial Medicine.*

Whereas there are about 50 natural isotopes, over 700 are now man-made. These artificial isotopes are increasingly being used in industrial processes and in medical diagnosis. The paper includes a useful table of the principal artificial isotopes, showing their half-life and type of radiations. Their applications and uses in medical diagnosis, medical therapy and research are briefly described in the text and illustrated by a series of informative diagrams.

C. C. LUCAS. *A Biochemist views Silicosis.*

Many hypotheses have been advanced to explain fibrogenesis in silicosis. The mechanical hypothesis has been rejected and the chemical solubility hypothesis is now regarded as inadequate. At present attention is focused on the investigation of the activities at the surface of silica crystals, that is the physicochemical-immunological interactions. In the incidental studies of enzymes and serum proteins the biochemist is playing an increasingly important part. These fundamental researches are important because when the biological process is understood, we are on the threshold of being able to arrest or even reverse it.

[This paper, to which is appended a comprehensive list of references, is a simple and lucid exposition of a very complex subject.]

G. W. H. SCHEPERS. *The Antidotal Capacity of Aluminium against the Histotoxic Action of Quartz.*

This study was completed at the Saranac Laboratory for the McIntyre Foundation. The purpose of the experiments was to evaluate the antidotal properties of 4 aluminium agents, one of which was McIntyre aluminium powder (M38) as now produced under controlled conditions. It offers further laboratory evidence of the efficacy of oxidized metallic aluminium in the prevention of silicosis and the work indicated that the finer particle size and great purity of the new powder may be still more efficient in countering the influence of silicon dioxide dust. The intrinsic inertness in animals of metallic particulate aluminium and oxidized aluminium is demonstrated. The paper is illustrated by excellent colour plates.

J. GOUGH. *The Lung in Collagen Diseases with special reference to Rheumatoid Pneumoconiosis.*

In the collagen diseases the lungs are frequently involved sometimes with specific changes but very often with non-specific lesions. Specific pulmonary changes have rarely been found in rheumatoid arthritis. CAPLAN [see this *Bulletin*, 1953, v. 28, 831], however, found that in coalminers with rheumatoid arthritis the radiographic changes of pneumoconiosis differed from those of coal miners without rheumatoid arthritis. This observation has since been confirmed by observers in many countries and in other dusty occupations.

[The pathology of rheumatoid pneumoconiosis has frequently been described by GOUGH and his colleagues, see *ibid.*, 1956, v. 31, 165.]

A. Meiklejohn

MINISTRY OF POWER. **Report of H.M. Chief Inspector of Mines and Quarries under the Mines and Quarries Act, 1954, for 1957** [ROBERTS, H. C. W.]. 71 pp., 5 pls. & 2 graphs. 1958. London: H.M. Stationery Office. [5s.]

——. **Report of H.M. Chief Inspector of Mines and Quarries under the Mines and Quarries Act, 1954, for 1958** [ROGERS, T. A.]. 62 pp., 4 graphs. 1959. London: H.M. Stationery Office. [3s. 6d.]

For some years previous to 1958 the accident statistics given in the Annual Report of H.M. Chief Inspector of Mines and Quarries dealt with the number of persons "reportably injured", a term which included not only persons who sustained serious bodily injury but also those who sustained lesser injuries as a result of certain dangerous occurrences. These minor injuries accounted for 15% to 20% of the total "reportable" injuries. In order to make more precise the incidence of serious bodily injury in mining and quarrying accidents, the statistics for 1958 and some earlier years have been adjusted to exclude these minor injuries. This means that current figures are restricted to persons whose injuries are severe enough to be reportable under section 116 of the Mines and Quarries Act, 1954.

During 1958, 327 persons were killed in coalmines; this is the lowest annual figure ever recorded. 1,752 men were seriously injured in 1958 as compared with 1,604 in 1957. The commonest cause of accidents, fatal and non-fatal, was falls of ground.

Commenting on the figures for new cases of pneumoconiosis the Chief Inspector, following the now standard warning on the validity of certification figures, states that the rate for 1958 was some 23% below that of 1957 and 40% below 1956. Relevant to this, scrutiny of table 6 shows that new cases in 1957 amounted to 3,756 and 2,902 in 1958, a fall of 854 cases. But the fall was not general throughout the country; the West Midlands division alone accounted for 521 (61%) of the decrease. In the much discussed South Western division, which includes South Wales, there was an increase of 63 cases.

There were 13,338 new cases of occupational diseases other than pneumoconiosis at coal mines. Beat knee, 7,916 cases, and dermatitis, 3,777 cases, were the chief contributors. Nystagmus cases amounted only to 83.

[As a frontispiece to the Report an outline map showing the boundaries of the colliery divisions would greatly assist readers. Confusion would be avoided if the divisions and geographical areas in tables 5 and 6 were assimilated. The Chief Inspector by his usage should establish the correct designation of East and West Midland(s) divisions; the National Coal Board and the Ministry of Power use Midlands.]

A. Meiklejohn

FAY, J. W. J. & RAE, S. **The Pneumoconiosis Field Research of the National Coal Board.** *Ann. Occup. Hyg.* London. 1959, Apr., v. 1, No. 2, 149–61. [27 refs.]

In 1952 the National Coal Board accepted an invitation by the National Joint Pneumoconiosis Committee to "undertake a field research to determine how much and what kinds of dust cause pneumoconiosis and to establish what environmental conditions should be maintained if mine workers are not to be disabled by the dust that they breathe during the course of their work" This research was to be a long-term survey over a period of at least 10 years at a representative sample of collieries. With these objects in mind the Pneumoconiosis Field Research was started by the Board and the project has since become known as the "twenty-five pits scheme".

The survey was carefully designed and planned based on the experience of previous scientific studies, particularly those carried out by the Pneumoconiosis Research Unit (PRU) of the Medical Research Council at Cardiff. Altogether 25 pits, originally 20, were chosen, 6 in South Wales, 5 in Scotland, 2 in Northumberland, 2 in Durham, 3 in Yorkshire and 1 each in Cumberland, North Wales, Lancashire, North Staffordshire, Warwickshire, Nottinghamshire and Kent. These pits were selected not on the basis of cases certified for Industrial Injury Benefits but on 4 factors, which were considered most likely to influence the problem. These were: (i) level of dustiness, (ii) rank of coal mined, (iii) presence of quartz in the strata associated with the coal seam, and (iv) ash content of coal seam *in situ*.

The scheme has 3 main components, medical, environmental and the correlation of these. The primary objects of the medical surveys are to determine the prevalence of pneumoconiosis and to study the occurrence and progress of the disease in the individual workmen and in colliery groups. The purpose is to radiograph on full-size film the population of the selected 25 collieries regularly every 4 years or so. Participation in the scheme is voluntary. In the first tour, completed in 1956, over 30,000 men representing 94·8% of the total pit populations were examined. In reading the films, which are classified according to the ILO classification, great care is taken to maintain consistent standards and to minimize inter- and intra-observer errors.

Concurrent environmental studies are designed to establish as accurately as possible the environment of each man under observation. The thermal precipitator is the standard sampling instrument. Since the inception of the surveys each item of the investigations has been kept under periodical review and the teams are satisfied that the original plan was satisfactory and is operating efficiently. Concurrent studies by the PRU and others have focused attention on the possible value of certain anthropometric indices and respiratory function tests and these have now been incorporated in the second tour.

The prevalence of pneumoconiosis, it is recorded, varies from very little significant pneumoconiosis at some collieries (1% of category 2 or more) to a considerable amount at others (about 20% of category 2 or more). Beyond this no results have been released for general information but these are promised "in due course".

117 persons, of whom 19 are medical, are employed full-time on the project. *A. Meiklejohn*

FAULDS, J. S., KING, E. J. & NAGELSCHMIDT, G. **The Dust Content of the Lungs of Coal Workers from Cumberland.** *Brit. J. Indust. Med.* 1959, Jan., v. 16, No. 1, 43–50, 6 figs. [10 refs.]

Dust analyses were carried out on 33 lungs of Cumberland coalworkers. The lungs were graded histo-

logically according to the classification of BELT and KING [this *Bulletin*, 1945, v. 20, 776]. 22 cases were graded 1 or 2 (simple pneumoconiosis), 5 as grade 3 (mixed nodulation) and 6 cases as grade 5 (silicotic nodulation). There were no cases of grade 4 (progressive massive fibrosis), in marked contrast to necropsy material from S. Wales coalworkers. Each grade of simple pneumoconiosis for the Cumberland lungs was found to contain more rock dust and less coal dust than those of S. Wales lungs [KING *et al.*, *ibid.*, 1956, v. 31, 641].

The results of the dust analyses are mainly expressed in terms of "percentage dried lung" although estimates of total dust content for both lungs are also given. [Presumably only one lung was analysed.] Mean total lung dust content increased with pathological grade but was not well related to mean period of dust exposure. Dust composition of the lungs correlated well with type of dust exposure. Only for grade 3 was the quartz content, as a percentage of total dust, significantly higher in the Cumberland lungs than in those of S. Wales but coal was the main constituent with less other dust in the S. Wales lungs.

["Mixed nodulation" is an unsatisfactory term and until the nature of different nodules can be more precisely identified a descriptive term such as "fibrous dust nodules" would be preferable. The paper is important in providing further evidence against the "quartz hypothesis" of progressive massive fibrosis. German workers please note.] *D. Rivers*

HARTMANN, W. L. Über die Silikose in der schweizerischen keramischen Industrie. [**On Silicosis in the Swiss Ceramic Industry**] [Thesis.] 90 mimeographed pp., 8 figs. [54 refs.] 1959. Zurich: Eidgenössichen Technischen Hochschule.

This paper is chiefly concerned with methods of dust measurement but it also gives results obtained in 15 locations in ceramic factories. The first part reviews theories of silicosis and lists the chief techniques used in various countries for dust measurement, for dust suppression and for silicosis control. Neither the Hexhlet nor the principle of size selection for collecting respirable dust is mentioned, but the theory of the thermal precipitator (TP) is discussed in detail. The review of dust-measuring techniques leads to the choice of TP, midget impinger and soluble filter combined with Gessner's sedimentation apparatus (SA) for experimental work. The last of these consists of collecting a dust sample on a filter, redispersing it in a liquid, and determining by micro-sedimentation analysis the proportion by weight of fractions of different sizes. SA has the advantage that the fractions can subsequently be used for mineral analysis but has the disadvantage that the state of aggregation of the particles in air is altered. It is the standard dust measuring technique in Switzerland.

For the experimental work a dust chamber of 14·5 m.^{3} (350 cubic feet) and a Wright dust feed mechanism were used. Quartz dust clouds were evaluated by TP, with light field illumination with phase contrast for counting. The lower limit of resolution was found to be 0·2μ. Simultaneous measurements with a British (Casella) and an Italian (Vaschetti) TP on 9 samples showed no significant difference in counts and a very high correlation ($r = 0{\cdot}99$) between the instruments. Further simultaneous measurements were made with TP, midget impinger and soluble filter (LE BOUCHET).

The midget impinger counts were intermediate between those of TP in the ranges 0·3–5μ and 1–5μ, but the 2 instruments gave significantly different results, probably on account of aggregation effects, and neither was highly correlated with the gravimetric data. On an average, 257 particles per cubic centimetre (ppcc), 1–5μ (TP count), corresponded to 1 mgm./m.^{3} of quartz dust but the values ranged from 52 to 423 ppcc. This is ascribed to variations, mainly, in larger particles in the cloud and to aggregation effects.

The above measurements had been made at an average concentration of about 1,000 ppcc, 1–5μ (TP), and the dust cloud had been led directly into the chamber. In a new series a settling chamber was interposed to remove aggregates as far as possible, and the dust concentration was increased.

A sample was taken on a paper filter in the Le Bouchet apparatus during 60 minutes and at the beginning and end of this period TP and sedimentation cell samples were taken. The sedimentation cell samples were allowed to settle for 22 hours (height not given) and 50 fields chosen at random were counted. The filter sample was ashed, its size distribution determined in the Gessner apparatus and particle number concentrations were obtained from the mass distribution by calculation. [It looks as if these calculations are carried out for spheres, and an empirical factor, designed to make the counts agree with TP results, is introduced instead of a shape factor.] 5 parallel series of measurements were made and evaluated.

In the size range 0·2 to 5μ the counts of TP and sedimentation cell gave similar average values of about 27,000 ppcc but the numbers of particles counted in the sedimentation cell were small and their variance was large. TP counts had a variance of ± 9% in the size range 0·2 to 5μ as compared with 23% for the size range 1–5μ.

The average mass concentration was 16 mgm./m.^{3} and the counts calculated from the size distributions were fairly constant with a mean of 1,845 ppcc, 1–5μ, which agreed well with the mean count of 1,778 ppcc of the TP samples for the same size range [see comment above], but the TP samples had a larger variance.

The numbers of ppcc in different size ranges corresponding to 1 mgm./m.^{3} of quartz dust were:

above 1μ	... ...	115 ppcc
„ 0·5μ	... ...	360 „
„ 0·2μ	... ...	1,710 „

Finally, the permeability of a soluble chloronaphthalene filter, of Whatman No. 1 and of a German paper filter (Schleicher & Schüll, 589, Blauband), were evaluated by measuring with a TP the dust passing the filters and by measuring the size distribution of the dust isolated from the filters. It was found that the German filter was the least regular in performance,

that it retained 97% or better of particles above 1μ and retained 30 to 70% of particles between 0·2 and 1μ. Both other filters retained over 99·5% of particles above 1μ and 75 to 80% of particles between 0·2 and 1μ.

A number of measurements with TP and filter apparatus (SA) in ceramic factories showed only rarely agreement of the TP counts in the 1–5μ range with particle numbers calculated from the filter dust weight and its size distribution. In general the calculated values were considerably higher (up to 10 times), probably on account of aggregation effects.

A comparison of the standard French method of dust evaluation (counting particles below 3μ obtained from soluble filter samples), with TP evaluation counting particles 0·5–3μ, gave for a set of 7 samples, on an average, good agreement, but poor correlation between the 2 methods (r = 0·34).

The experimental results are followed by a discussion of maximum allowable concentrations and it is shown how a given set of measurements would be assessed in different countries by different methods, assuming the sample had 50% of quartz and only a few aggregates. Soluble filter, midget impinger and TP counts in the range 0·5–5μ led to similar assessments; an unpublished [and perhaps misunderstood] Dutch standard was considerably more stringent and a tentative Swiss standard much more lenient.

[The author is, incidentally, under the impression that the "approved conditions" for rock work in British coal mines allow 450 ppcc, 0·5–5μ, of rock dust with up to 50% of quartz *and* 650 ppcc, 1–5μ, of coal dust; pp. 61, 64.]

A lengthy discussion on aggregates follows in which it is considered that aggregates should be counted as single particles and that discrepancies between midget impinger or filter plus SA "counts" and TP counts on the same dust cloud give an estimate of the degree of aggregation.

In other words, the filter method exaggerates the dust hazard the more the larger the number of aggregates is.

In the second part of the paper silicosis statistics for about 900 men employed in 6 ceramic factories are given. There were 20 compensation cases; in 12 of them the men had died. The exposure times at first certification and the times at which the men got a higher assessment of disability or died are shown in 2 graphs. German data are quoted for comparison and it is concluded that they do not differ significantly.

Dust measurements with TP were made in different working places in ceramic factories and large but unpredictable variations in counts 0·2–5μ were found at different times of day or at different days in a given place and also for different places. A number of detailed results of such measurements are given and discussed. *G. Nagelschmidt*

NORVIIT, L. Silikos i Laisvall. **[Silicosis at Laisvall]** *Nordisk Med.* 1959, July 16, v. 62, No. 29, 1076–81.

The English summary appended to the paper is as follows:—

"An investigation of the silicosis problem at the Laisvall lead mines is presented. The mined ore contains 80—90 per cent of quartz. The mine was opened in 1942. During the first few years the dust concentration in their air at the places of work was calculated much more than 1,000 particles per ccm. Between 1949 and 1952 steps were taken to reduce the dust content and, since then, the density has been 100—200 particles per ccm.

"The investigation comprises all the 504 persons who up to the end of 1957 had worked for at least 2,000 hours in places where there was a risk of their contracting silicosis. 45 cases of silicosis were registered among these workers.

"The working time used as the basis for the calculations is the time in hours during which the subject was exposed to stone dust.

"Making allowance for the comparable exposure time and period of observation up to the present, the incidence of silicosis has fallen from 45 per cent of 76 exposed persons during the first, worse period to 0 out of 103 during the later, better period.

"By an analysis of the cases of silicosis it is found that two-thirds of all cases were mild, while nearly one-third showed rapid progression of the disease. It is concluded that non-complicated Laisvall silicosis is of a mild character and the tendency to progression slight. The severe nature of the advanced cases is due mainly to complication with tuberculosis."

LEHIR, M., GUERRERO, A. & VAN RYCKE, J. La silicose au Maroc. **[Silicosis in Morocco]** *Arch. Malad. Professionnelles.* Paris. 1959, May–June, v. 20, No. 3, 333–41.

In Morocco there are 5 principal mining areas comprising a wide variety of minerals, coal, lead, pyrites, iron-ore, phosphates, manganese and cobalt. These minerals are of considerable value to the economy of the country but mainly as exports for there are few industries in which they can be utilized.

At the request of the Ministry of Industrial Production and Mines and the Chamber of Mines the tuberculosis service conducted an inquiry throughout the country to discover the incidence of silicosis in the various mines. The investigations included radiographic examination of the chest and tests of pulmonary function.

Among 36,249 workmen examined, 302 cases of silicosis and 282 cases of active tuberculosis were diagnosed. It emerged that the problem was not universal throughout the mining industry but was restricted to 3 mines. At Djerrada coalmine 209 cases of silicosis occurred among 4,866 workmen; at Aouli lead mine there were 56 among 843 workmen, and at Bou Azzer cobalt mines 10 in a population of 772.

The problem is not regarded as serious as only about 7,000 miners are at risk and the annual yield of new cases in the next few years is expected to be between 30 and 40. The authors recommend modification of existing legislation and provision of regular medical supervision and environmental control by mining engineers. *A. Meiklejohn*

AYRE, W. B. **Silicosis in the Foundry—Medical Control.** *Arch. Indust. Health.* Chicago. 1959, May, v. 19, No. 5, 490–96.

At a large steel foundry in Canada 153 cases of pulmonary fibrosis were diagnosed during the 45 years 1912–57. [In 1942 silicosis became compensatable as an industrial disease in the Province of Quebec.] Of these 153 cases, 23 were diagnosed as siderosis, 37 as non-specific fibrosis and the remaining 93 as silicosis, grade I, 33, grade II, 22, and grade III, 38. Among the silicotics 19 deaths have occurred, 3 from extraneous causes and 16 in some measure directly attributable to the pulmonary disease; 7 of the 16 died of tuberculosis. After diagnosis of the disease many of the patients were able to continue in full work in the foundry. The occurrence of silicosis varied in different departments of the foundry, being most common among workmen engaged in cleaning processes, chipping (fettling) and grinding. Pulmonary tuberculosis was the most important problem in medical control, which aims to delay the onset of disability and minimize it when it occurs. Accordingly early detection and prompt treatment are important. The author suggests that the criteria for antibiotic therapy of silico-tuberculosis should be broadened. He also underlines the importance of being aware of the possible onset of cardiac complications and the value of electrocardiography.

[This is a general statement of a personal experience of pulmonary disease in a steel foundry. It accords with that of others and is almost entirely a repetition of accepted facts.] *A. Meiklejohn*

VIGLIANI, E. C. & PERNIS, B. **An Immunological Approach to Silicosis.** *J. Occupational Med.* Chicago. 1959, June, v. 1, No. 6, 319–28, 8 figs. [50 refs.]

This article is almost identical with one in *British Journal of Industrial Medicine*, 1958, Jan., v. 15, No. 1, 8–14 [this *Bulletin*, 1959, v. 34, 347]. *A. Meiklejohn*

PERNIS, B., GAMBINI, G. & FINULLI, M. Le immunoconglutinine nel siero dei silicotici. [**Immunoconglutinin in Silicotic Patients**] *Med. d. Lavoro.* 1959, Apr., v. 50, No. 4, 250–56, 2 figs. [10 refs.]

The English summary appended to the paper is as follows:—

"Immunoconglutinins may be considered, after MARKS and COOMBS (1957, J. Hyg., *55*, 81 [this *Bulletin*, 1957, v. 32, 820]), as autoantibodies directed against the organism's own complement; they are produced, as a secondary immune reaction, when antigen-antibody reactions with fixation of complement take place 'in vivo'. Therefore the serum immunoconglutinin level is somehow related to the general immunological activity of the organism.

"MARKS and COOMBS write that 'if in any particular disease of unknown origin a constantly raised level of immunoconglutinin was found it would indicate that an antigen-antibody interaction was involved in the aetiology'."

"The Authors have determined the immunoconglutinin level in the serum of 66 patients with active silicosis and without associated infection: in 88% of these cases this level was above the upper normal one of 1 : 4 and almost one half of the cases had titers ranging from 1 : 32 to 1 : 128. This distribution of immunoconglutinins amongst silicotics is similar to that found by MARKS and COOMBS in cases of active rheumatoid arthritis and is a further support of the role played by immunologic reactions in the pathogenesis of silicosis as assessed by previous research work of VIGLIANI and PERNIS (1958)."

MARCHAND-ALPHANT, A. & GRAILLES, M. Faciès anatomopathologique des pneumoconioses des Houillères du Bassin du Nord et du Pas-de-Calais. [**Histological Appearances of Pneumoconiosis among Coalminers in the Nord—Pas-de-Calais Coalfields**] *Rev. Méd. Minière.* Sin-le-Noble. 1959, v. 12, No. 40, 33–42, 13 figs.

On May 27, 1954, Fruhling and Chaumont read a paper at the Congress of Occupational and Medico-Legal Medicine, held at Strasbourg, on the histological appearances of pneumoconiosis as observed by them among coalminers in the Lorraine coalfield. This stimulated the present authors to make a similar study in the Nord—Pas-de-Calais coalfields.

Pathological material was obtained from necropsies, some after exhumation, performed for medico-legal purposes during the years 1952–8. Paraffin sections were prepared and appropriately stained with a variety of dyes for microscopic examination. For investigation of the nature and quantity of the included dust, sections were micro-incinerated after treatment with hydrochloric acid.

1,086 cases were investigated and the histological lesions were classified as follows:

silicosis	800
silico-tuberculosis	200
coalworkers' pneumoconiosis (Gough) ...	86

Analysis of the 800 cases classified as silicosis showed that discrete nodular lesions occurred in only 17% of cases; confluent and massive fibrosis—complicated pneumoconiosis—accounted for the remaining 83%. In 390 (49%) cases cavitation was present; significant emphysema in 57% of cases and primary bronchial carcinoma in 3% of cases.

In the 200 cases of silico-tuberculosis massive lesions were present in 66·5% of cases, and nodular lesions in 30·5%. Massive fibrosis occurred in only 6% of the 86 patients with coalworkers' pneumoconiosis and tuberculosis occurred as a complication in 1 only.

Acute inflammatory complications were more common in silicosis (22%) than in coalworkers' pneumoconiosis (16%).

The authors admit that the material was "selected" so that the above figures do not provide an absolute measure of the relative prevalence of the separate forms of pneumoconiosis. They do, however, provide a general view.

The article is illustrated by a series of photomicrographs. *A. Meiklejohn*

OTTO, H. & MARON, R. Zur Histologie der Eisenablagerungen bei Porzellinersilikosen. [**The Histology of Iron Deposits in Silicotic Lungs from the Pottery Industry**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 2, 117–26, 3 figs. (1 coloured).

The paper is based on histological observations of 40 silicotic lungs from subjects who had acquired the disease in the glass and procelain (hard china) industry. Serial sections were stained with haematoxylin and eosin and by Turnbull or Berlin Blue methods of staining for iron. Both iron stains gave very similar results.

Lung and lymph gland sections were examined. A general diffuse accumulation of iron was observed in dust cell granulomata and on the outer rims of silicotic lesions; the hyaline centres did not contain any iron. The iron is believed to be haemosiderin developed from haemoglobin, and most or all of it is said to be endogenous. When confluence of lesions occurs the iron is pulled outwards. Near the dust deposits many alveolar epithelial cells filled with haemosiderin may occur. These are believed to be the result of local blockage of blood flow.

In the lymph glands, as in the lungs, the hyaline centres of silicotic nodules are free from iron but much iron is found in neighbouring parts of intact lymph tissue.

There is a long discussion on the origin of the iron which is said to be the result of local interference with blood circulation. Anthracotic town dwellers' lungs do not show such haemosiderin, and a certain development of pneumoconiotic lung damage is necessary before iron deposits are found. The iron in the alveolar epithelial cells is said to be a sign of lung congestion and such cells are found only in advanced stages of disease.

In tuberculosis, iron deposits were neither found in freshly exudative nor in chronic indurative cases, and hence the occurrence of iron is said to be of less diagnostic value than measurement of the amount of dust isolated from the lungs. The paper is illustrated by one coloured and two black and white figures.

G. Nagelschmidt

GUYOTJEANNIN, C. & GUYOTJEANNIN, N. L'hypercoagubilité du sang dans la silicose. [**Increase in Coagulability of the Blood in Silicosis**] *Arch. Malad. Professionnelles.* Paris. 1957, Sept.–Oct., v. 18, No. 5, 553–7. [Refs. in footnotes.]

In the course of an investigation into the changes in the proteins of the blood in silicotic patients, measurements were made of the amount of prothrombin, which is a glycoprotein. The technique used was that described by QUICK in 1938. 25 patients with silicosis were tested and in 24 there was an increase in prothrombin; in 18 the amount exceeded normal by 15% to 35%. In the same 24 patients it was found that the recalcification time of Howell was diminished. These findings are interpreted as indicating an increase in the coagulability of the blood in silicosis.

A. Meiklejohn

FOURNIER, E. & GUYOTJEANNIN, C. Le Test de Ducci (rouge colloidal) dans la silicose. [**The Ducci (Colloidal Red) Test in Silicosis**] *Arch. Malad. Professionnelles.* Paris. 1957, Sept.–Oct., v. 18, No. 5, 548–52.

The Ducci test is a flocculation reaction between blood serum and a solution of colloidal red. In making the test the *p*H values, 7·35 to 7·45, must be strictly observed. The test so far has been used, particularly in diseases of the liver, to detect early fibrotic changes. The authors, having observed that the test was of some value in detecting the development of fibrotic changes in tuberculosis of the lungs, considered that it might similarly be of use in silicosis.

34 cases of silicosis were investigated; 28 cases of nodular silicosis, 2 of massive fibrosis and 4 of bacteriologically confirmed silico-tuberculosis. The Ducci reaction was positive in 13 cases. These were further investigated by other serological tests, involving α, β and γ globulins but no positive correlation was found between any of the results.

A. Meiklejohn

GUYOTJEANNIN, C., FOURNIER, E. & GAGER. Le Test de floculation de Sandor dans la silicose. **Sandor Flocculation Test in Silicosis**] *Arch. Malad. Professionnelles.* Paris. 1957, Sept.–Oct., v. 18, No. 5, 568–70. [Refs. in footnotes.]

DI GUGLIELMO, L., SALVINI, M. CATTANEO, L. **Isolated Lymph-Gland Silicosis.** *Scientia Med. Italica.* 1959, Apr.–June, v. 7, No. 4, 743–57, 5 figs. [30 refs.]

DECROIX, G. & MATOSSY, Y. Silicose précoce apparue après 4 mois d'exposition au risque silicogène. (A propos d'une observation.) [**A Case of Silicosis Occurring after 4 months' Exposure**] *Arch. Malad. Professionnelles.* Paris. 1959, May–June, v. 20, No. 3, 254–7. [21 refs.]

Early in October 1957, a workman aged 34 years was admitted for investigation to the medical unit of Professor R. Kourilsky at the Saint-Antoine Hospital, Paris. The patient was referred by the medical officer to a public works organization. In the course of routine X-ray examination of the chest the doctor had observed miliary shadows throughout the lungs. Very thorough clinical and clinico-pathological tests, with special reference to tuberculosis, revealed no abnormality apart from the reticulo-micronodulation in the lungs.

For a period of 4 months, February to May, 1957, the workman was employed in drilling and boring tunnels through solid rock. In addition to the inhalation of dust he was exposed to fumes from explosives. Investigation of the employment history proved that this period of 4 months represented the patient's total exposure to any dust risk. This exceedingly short period made the doctors very guarded and despite the evidence against tuberculosis the patient was treated for 35 days with streptomycin, isoniazid and PAS. The sputum remained persistently negative for tubercle bacilli and pulmonary function tests were normal.

The radiographic appearances remained unaltered by treatment. Lung biopsy was then undertaken. Histological examination of the material established the presence of silicosis and silica was found by chemical examination after micro-incineration.

To account for such a rapid onset of the silicosis the authors think that the reaction to silica dust may have been facilitated and accelerated by irritation of the lungs by gases arising from explosives.

[The value of this case report would have been greatly enhanced by details of the rocks and dust clouds. Such cases seldom occur singly and so it is hoped that the workmen on this project will be kept under close scrutiny over the next few years. In Great Britain cases of acute silicosis have been observed but usually the disease has been of the complicated variety—PMF. Again these cases have only become overt after a latent period of 1 to 2 years. The present case is of extreme interest because the disease developed and presented radiographically within a total period of 8 months.] *A. Meiklejohn*

DELESVAUX, R. Diagnostic précoce du retentissement cardiaque de la silicose. [**The Early Diagnosis of Cardiac Complications in Silicosis**] *Rev. Méd. Minière.* Sin-le-Noble. 1959, v. 12, No. 40, 3–31, 8 figs. (1 folding).

Between 1951 and 1958, 71 cases of chronic cor pulmonale were investigated among miners suffering from silicosis from the Béthune area of France. Close questioning of patients, whose incapacity from silicosis amounted to 65% or more, revealed that there were 4 main groups of symptoms and signs which ought to lead the doctor to suspect the possible onset of cardiac insufficiency.

(1) Recurrent attacks of acute respiratory affection and aggravation of chronic purulent pulmonary conditions. These episodes, it was observed, were most liable to provoke cardiac complications during the winter months.
(2) Concurrent chronic bronchitis.
(3) Extent and severity of the silicosis, particularly the development of massive fibrosis and perifocal emphysema.
(4) Sudden degeneration of fibrotic areas; by contrast slow cavitation did not seem to induce serious cardio-vascular changes.

Clinical study of the patients underlined the importance of recent onset or sudden aggravation of dyspnoea when lying down; accentuation of the 2nd pulmonary sound; cyanosis; hypoxaemia; and persistent tachycardia after prolonged rest. The further investigations included tests of pulmonary function, radiology of heart and lungs and electro-cardiography. The authors identified two syndromes.

Syndrome of Suspicion. This includes disturbances of breathing, accentuation of 2nd pulmonary sound, occasionally cyanosis and pulsation of right heart. At this stage abnormal radiological signs are not prominent and ECG changes are equivocal. The maximal voluntary expiration per second (VEMS) is always diminished.

Syndrome of Certainty. This comprises recent cardiac enlargement diminished VEMS and typical ECG pattern.

The article is illustrated by the radiographs and ECG tracings of 8 cases.

Early diagnosis is of great importance as the cardiac complications may respond to general and specific therapy. *A. Meiklejohn*

JAHN, R. P. **Silicosis and Avian Tuberculosis.** *Amer. Rev. Respiratory Dis.* 1959, July, v. 80, No. 1, Pt. 1, 78–84, 4 figs.

"In a case followed for twenty-one years, the development of silicosis and a superimposed infection was observed. In addition to a positive avian tuberculin test, atypical acid-fast bacteria were recovered repeatedly and constantly over a ten-year period. These bacilli with cultural qualities, agglutination studies and drug-resistant patterns typical of avian tubercle bacilli showed consistent inability to infect a guinea pig and ability to infect fowl."

VIGLIANI, E. & SARTORELLI, E. Terapia delle forme confluenti di silicosi. [**Treatment of Confluent Forms of Silicosis**] *Med. d. Lavoro.* 1959, Apr., v. 50, No. 4, 245–9.

The English summary appended to the paper is as follows:—

"The criteria adopted in the Clinic for Occupational Diseases of the University of Milan for the treatment of massive forms of silicosis are described. This treatment includes: 1) treatment of respiratory insufficiency and possible right cardiac failure; 2) treatment of chronic bronchial infections and of intercurrent acute broncho-pulmonary infections; 3) finally, in cases with a rapid and malignant course, administration of cortisonic drugs together with antitubercular drugs. The treatment of respiratory insufficiency consists of controlled oxygen administration, breathing helped by mechanical respirators, administration of cardiac tonics, acetazolamide and respiratory analeptics. Bronchial and pulmonary infections are treated with wide range antibiotics by aerosol or by general administration. Among cortisonic drugs, prednisone and now also desametazone are preferred; they are given in association with isoniazid which is one of the best tolerated antitubercular drugs."

NADUDVARY, G., ROSENFELD, C., BERNSTEIN, R., BALKANYI, N., RADIOVOIU, T., WEISZ, A. & WEINBERGER, I. Prevenirea silicozei prin folosirea unei noi substanțe umectante pe bază de bentonită la perforajul mecanic umed în mină (substanța "B"). [**The Prevention of Silicosis by the Use of a New Wetting Material based on Bentonite for Wet Mechanical Drilling in the Mining Industry**] *Igiena.* Bucharest. 1958, July–Sept., v. 7, No. 3, 213–18, 6 figs.

An investigation has been made of the efficacy of bentonite added to the drilling water in the reduction

of the dust content of the air during wet drilling operations in a mine in Rumania carried out in pegmatite containing 89% of silica. The mean number of particles in air samples taken during dry drilling was 38,071 per ml.; during wet drilling with plain water the dust content fell to 962 particles per ml. and this was further reduced to 66 and 57 per ml. by the respective addition of 0·5% and 2% of bentonite to the drilling water. The use of bentonite reduced the proportion of dust particles less than 1μ in diameter from 40% to nearly 20%. *D. J. Bauer*

SCHERRER, M. Neues Verfahren zur Stabilisierung des O_2 am Metabographen von Fleisch. [**A New Method for the Stabilization of Oxygen in the Fleisch Metabograph**] *Bull. Schweiz. Akad. Med. Wiss.* 1959, May, v. 15, Nos. 2/3, 145–63, 14 figs.

The English summary appended to the paper is as follows:—

"The volume-directed O_2 stabilisation of the Metabograph of *Fleisch* has the disadvantage that shifts of the expiratory position lead to errors of measurement of the oxygen consumption and to variations of the oxygen content of the inspiratory air up to 2 vol.%. A new procedure for the stabilisation of the oxygen is described, whereby the continual oxygen supply in the Metabograph is regulated on the basis of the N_2 content of the air of the system. In continual measurement of the N_2 content, the nitrogen meter of *Lilly* is used. Even with irregular respiration of the experimental person, during work tests, it is possible to keep the N_2—O_2 content of the inspired air constant to $\pm$ 0.2 vol.%. Simultaneously with the testing with the Metabograph, the arterial blood can also be determined for O_2 and CO_2 tension and the alveolo-arterial O_2 tension difference can be measured."

GOBBATO, F., ZAGARESE, G. & ALFIERI, E. Modificazioni della sistole isotonica in funzione della frequenza cardiaca durante e dopo prova da sforzo. [**Changes of the Isotonic Systole as a Function of Cardiac Output during and after Effort**] *Med. d. Lavoro.* 1959, Apr., v. 50, No. 4, 264–72, 5 figs. [12 refs.]

The English summary appended to the paper is as follows:—

"Sphymographic tracing was registered on the carotid artery in normal subjects during effort on a cycloergometer and the behaviour of isotonic systole was analysed during the phases of the test. Both correlation coefficient and regression function between ventricular expulsion time and pulse rate were calculated during effort and immediately afterwards (restorative phase). It was observed that, for the same pulse rate, the expulsion time lasts longer during muscular exercise than during the restorative phase: it is assumed that this is due to the increased output in such conditions. Variations of diastole duration during effort are defined and their possible effects on cardiac dynamics are pointed out."

GOBBATO, F., SEQUI, G., ZAGARESE, G. & BERRA, A. Modificazioni emodinamiche indotte dalla ipoosia in pneumoconiotici. (Osservazioni sul Test di Levy.) [**Haemodynamic Changes induced by Hypoxia in Pneumoconiotic Patients (Observations on Levy's Test)**] *Med. d. Lavoro.* 1959, Apr., v. 50, No. 4, 273–85, 5 figs. [Numerous refs.]

The English summary appended to the paper is as follows:—

"Circulatory response to hypoxia in patients with pulmonary silicosis was analyzed after inhalation of low oxygen mixtures (10% Oxygen in nitrogen) for periods of 16 to 22 minutes. The results showed that: *a*) during hypoxia there is a marked increase of cardiac output mainly due to increased frequency rather than to increased systolic output. Hypoxia also induces a systemic arterioles vasodilatation with decreased peripheral resistance; *b*) hemodynamic function is more sensitive in subjects with impaired respiratory function; *c*) hypoxia test can be recommended not only to reveal a latent coronary disease in subjects with suspicious symptoms but normal EKG 'at rest', but it can also be used to visualize the EKG signs of an incipient right heart impairment in subjects with chronic pulmonary disease."

SARTORELLI, E., MAGISTRETTI, M., PEIRONE, E., GRIECO, A. & GRIMALDI, M. G. Validità della misura della saturazione in O_2 del sangue arterioso *in vivo*, a riposo e in lavoro, con l'ossimetro Waters X-80 A. Studio in soggetti normali, silicotici, enfisematosi e tubercolotici. [**Reliability of the Determination of Arterial Blood Oxygen Saturation (A.O.S.) *in vivo*, at Rest and during work, with the Waters X-80 A Oximeter. A Study on Normal, Silicotic, Emphysematous and Tuberculous Subjects**] *Med. d. Lavoro.* 1959, Apr., v. 50, No. 4, 286–300, 2 figs. [Numerous refs.]

The English summary appended to the paper is as follows:—

"The arterial oximetry in vivo, at rest and during work has been criticized by some authors from both technical and theoretical standpoints. It seemed therefore interesting and a more careful study on the reliability of the determination of a.o.s. at rest and during work was carried out with a transmission type oximeter (Wood Waters X-80 A). The percentages of a.o.s. obtained in vitro with the cuvette of the oximeter have been statistically tested (Student't) with those given by the Nahas spectrophotometric method which has been proved to be certainly reliable by other researches. The results obtained by the two methods agreed quite closely. A study has been then made on the reliability of in vivo determination of a.o.s. at rest with the ear oximeter Waters X-80 A, by statistical comparison with the corresponding values obtained in vitro with the cuvette of the oximeter. This study made on 55 normal or lung-diseased subjects showed a good reliability of the determination of the a.o.s. in vivo and at rest made with the oximeter. Finally a study has been made on the

reliability of the determination of the a.o.s. in vivo with the Waters X-80 A oximeter by statistical comparison with corresponding values obtained by arterial oximetry in vitro. 172 comparative determinations of the a.o.s. have been made during work tests of different intensity on 55 subjects: 10 normals, 21 with silicosis of various grades, 12 with more or less advanced emphysema. 12 with tuberculosis (some of these with history of chest surgery). The a.o.s. in vitro has been taken by incanulating the brachial artery with a Cournand needle which was maintained in situ by putting the arm in a stick shower-bath during the work tests. The last ones consisted of a 15% grade walk at various speeds on a treadmill. This study showed that the determination of the a.o.s. in vivo is reliable also during work tests even if those are made at the high level of intensity. The determination of the a.o.s. in vivo with Waters X-80 A oximeter is therefore a reliable method which may prove very useful for research and for investigations on respiratory function at rest and during the work in lung-diseased patients for legal and insurances purposes."

PATERSON, M. S. & WHEATLEY, K. **Solubility and Heat of Wetting of Silica Powders.** Reprinted from *J. Applied Chem.* 1959, v. 9, 231–40, 3 figs. [20 refs.]

The paper gives the results of silica solubility determinations and other physico-chemical studies of a number of fractions of graded size of quartz and other modifications of silica. The studies were undertaken in order to correlate physico-chemical properties with fibrogenic activity found in animal experiments.

The materials studied were very pure quartz from Madagascar and less pure quartz from Belgium and Scotland (Loch Aline sand); fused silica, cristobalite and tridymite prepared from Madagascar quartz were also examined. The diameters of the graded fractions ranged for quartz from 0·5 to 500μ and for the other silica modifications from 0·5 to 4 or 8μ.

Silica solubility was determined in such a way that mono- or low-polymer silicic acid which reacts rapidly with ammonium molybdate (AMR silica) could be distinguished from polysilicic acid or mineral particles which do not react. The specific surface of the samples was determined by optical or electron microscopy and by low-temperature gas adsorption, and the heat of wetting by water was also determined on a number of samples.

It was found that all samples released AMR silica only into solution. Conflicting views of earlier investigations could be explained as due to the presence of mineral particles of colloidal size. The rate at which the AMR silicic acid was released depended on the amount of surface present and on particle size; at equal surface it was roughly the same for the different silica modifications. [Fig. 1a suggests that vitreous silica had the highest rate.] The solubility of the less pure quartz samples was lower than that of quartz from Madagascar and it was proportional to the amount of surface present irrespective of size. The purest quartz had, per unit surface, about 3 times higher solubility with particles below 3μ than with larger particles.

X-ray diffraction results are quoted which suggest that ground quartz has a disturbed layer and that the proportion by weight of this layer will increase as the particle size decreases. Tridymite does not show this effect. Repeated extractions with Ringer's solution suggest that quartz, tridymite and vitreous silica of Stokes size 0·5–2μ contain between 2 and 4% of material which is more soluble than the remainder. Samples of all silica modifications etched with hydrofluoric acid had considerably lower solubilities than unetched samples. Heat of wetting with water gave a constant value per unit surface of quartz, irrespective of particle size or whether or not the samples had been etched.

The main conclusion of the work is that the easily soluble silica does not appear to play an important part in silicosis. The findings are also used to explain certain discrepancies in the literature.

G. Nagelschmidt

DRÖSSLER, H., SZONGOTT, M., PANZER, E. & KITZLER, W. Über die Ermittlung der "kritischen Staubdichte" in Österreich. **[On the Determination of "Critical Dust Concentrations" in Austria]** *Staub.* Düsseldorf. 1959, Aug. 1, v. 19, No. 8, 288–90, 2 figs. [12 refs.]

The paper describes very briefly the criteria which are used for assessing the pneumoconiosis hazard of dusts. It is a combination of American (MAC) and German (LANDWEHR) ideas and takes account of composition, concentration and size distribution of dust.

Dust composition is determined on samples of airborne dust, if possible of respirable size, and is evaluated according to Landwehr's scheme [this *Bulletin*, 1958, v. 33, 669]. Dust concentration is the number of particles per cc. from konimeter samples evaluated by dark-field counting at a magnification of × 1,080.

For size distributions below 3 microns all dusts are classified as coarse, medium and fine with mean diameters of 2, 1·2 and 0·7 micron and surface values in approximate proportions of 1 : 3 : 7. This is done in order to base the assessment of hazard on surface rather than number or mass. Number and surface size distribution curves and typical dark-field photographs for the 3 dust types are given.

The dust assessment factor is $x = \frac{TG}{100\,K}$, where T is the number of particles per cc., G is the dust composition factor which ranges between 5 and 100, and K has the value of 4·2 for fine dust, 2·4 for normal dust and 0·9 for coarse dust.

Values of x below 100 are considered as safe, above 150 dangerous, and between 100 and 150 they are "critical". The assessment is, however, said to be dependent on the experience of the observer and in practice arbitrary dust standards are prescribed in different industries. The present note is presented in order to stimulate discussion. *G. Nagelschmidt*

TOMIC, A. Narodno zdravlje i higijenski faktori na području rudnika i fabrike azbesta. [**Public Health and Hygienic Factors in the Region of an Asbestos Mine and Factory**] *Higijena.* Belgrade. 1958, v. 10, No. 4, 273–86. English summary.

An investigation has been made of the hygienic conditions in the environs of an asbestos mine and factory in Yugoslavia. Among 76 workmen seeking medical attention who were examined radiologically 22 (28·9%) were suffering from asbestosis, 29 (38·2%) from anthracosilico-asbestosis and 2 (2·6%) from anthracosilicosis. The dust content of the air in the factory ranged from 5 to 550 mgm. per cubic metre, and the total daily atmospheric deposit at various points in a village situated 600 metres from the factory ranged from 203·5 to 996·6 mgm. per square metre.

D. J. Bauer

CLAUSEN, Kay H. **Talcosis in a Rubber Factory.** *Acta Tuberculosea Scandinavica.* 1959, Suppl. 47, 60–61.

During 1957 about 1,200 workers in a rubber factory were X-rayed by a mobile unit, "Odelca 70 mm.". Definite talcosis was diagnosed in 9 cases, average exposure 19 years, range 7–30 years, and slight talcosis 7 cases, average exposure 12 years, range 0–25 years. Even in patients whose lungs revealed definite lesions, nodules up to 5 mm. in diameter, only 3 had symptoms, cough, expectoration and dyspnoea. It was noted that while some workmen developed gross lung lesions after many years of exposure to talc dust, other workmen after the same exposure showed no abnormal radiographic changes.

[This article is a very brief statement of findings, without detailed analysis or discussion. Apart from the figures given above, there is no information for the research worker in this field.] *A. Meiklejohn*

MOSCHINSKI, G., JURISCH, A. & REINL, W. Die Lungenveränderungen bei Sinterhartmetall-Arbeitern. [**Lung Changes in Hard-Metal Workers**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 16, No. 6, 697–720, 8 figs. [26 refs.]

The total population in 4 factories processing hard metals was investigated clinically and radiologically. Of the 326 people examined, there were 20 who showed the earliest radiological changes of pneumoconiosis (increased lung marking), 38 showed slight changes, and there was 1 with severe lung-fibrosis. Most of the subjects with pneumoconiosis were moulders or mixers; only a few were sinterers. Lung disease appeared to be associated with the processes which precede sintering of the hard metal. There were also 3 cases of slight pneumoconiosis in titanium workers. Environmental studies of the dust content in the factories were made with gravimetric and volumetric dust-sampling instruments. Airborne dust concentrations in the respirable size range were estimated separately for the various phases of processing the hard metals. A high incidence of bronchitis is claimed for hard-metal workers. [No control studies are mentioned.] There was no clear correlation between period of exposure, dose of dust, and development of lung changes. An allergic-hyperergic reaction to hard metal is suggested.

D. Rivers

HUSTEN, K. Hartmetall-Fibrose der Lunge. [**Hard-Metal Fibrosis of the Lung**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 16, No. 6, 721–32, 5 figs.

The author gives a detailed clinical and pathological description of one case of interstitial lung fibrosis probably due to inhalation of hard metal particles. Lung disease due to the hard metals is not prescribed in Germany.

D. Rivers

HORIUCHI, K. & HORIGUCHI, S. **Studies on the Industrial Lead Poisoning. I. Absorption, Transportation, Deposition and Excretion of Lead. 5. An Experimental Study with Radioactive Lead (Radium D).** *Osaka City Med. J.* 1958, Jan., v. 4, No. 2, 159–70, 6 figs. [21 refs.]

Guineapigs, given Pb acetate solution for about a month until lead-poisoned, were given a solution containing some Pb acetate and a radioactive lead tracer (Ra D) either subcutaneously, group 1, or orally, group 2, or intratracheally, group 3. The dose of Ra D solution (10 microcuries/kgm. of Ra D) was 1 mgm./kgm. Serial Ra D measurements were made for 20 days to compare distribution and excretion.

Blood Ra D concentrations reached maximum quickly, lowest in group 2, highest in group 1, and began to fall rapidly on the 2nd day. The red cells contained most, plasma and serum very little.

Tissue distributions were measured in ashed samples, allowed to equilibrate for a month, from animals killed by bleeding about every 5 days from the 3rd day. Ra D concentrations were of the following order, disregarding amounts at administration sites: group 1, bones highest, especially the flat bones, in early and late specimens; liver, spleen and kidneys high early, low by the 10th day; lung low, increasing later; group 2, bones and teeth highest; next liver, rapidly decreasing and spleen, gradually; kidneys low, gradually increasing; group 3, kidneys highest; bones and teeth next; liver and spleen high, decreasing gradually; caecum relatively high and remaining so. Very little was found in other organs in any group.

Excretion, estimated each day, was greater in faeces than urine except in group 1 during the first 3–4 days. In both parenteral groups urinary and faecal concentrations decreased gradually and in the oral group the much higher faecal concentration decreased rapidly for about 2 weeks. Cumulative excretion ranged as follows from the end of 3 or 4 days to the 19th or 20th: group 1, total Ra D 4%–20% (urinary 3–11%, faecal 1–10%); group 2, 76%–87% (0·5–2%, 73–85%); group 3, 12%–46% (5–12%, 6–35%).

Absorbed Ra D, the remainder after deducting amounts excreted during 20 days and the amount in the administration site on the 20th day was: group 1, 24·3% (urine 10·7%, faeces 9·6%, injection site 56·4%);

group 2, 5·3% (2·1%, 84·1%, gastrointestinal tract 8·5%); group 3, 31·8% (11·3%, 34·8%, trachea and lungs 22·1%).

There appeared to be a relationship between the amount of Ra D absorbed and the amount excreted in the urine, and it is suggested that if urinary Pb excretion is measured the amount of Pb absorbed can be approximately estimated (presumably if time and other factors are known). *M. Patricia Fitzsimons*

MARMET, J. Industrietoxikologische Untersuchungen bei Bleiarbeitern **[Toxicological Investigations in Lead Workers]** [Thesis] 128 pp., 28 figs. [205 refs.] 1958. Zurich: Eidgenössischen Technischen Hochschule.

After a brief description of the physiological and pathological properties of lead, an exhaustive enquiry is made into working conditions and potential hazards in 3 electric accumulator and 3 lead colour factories, and a machine shop in Switzerland. This includes chemical and biological analyses of the lead concentrations in the air of the various departments and in the blood and urine of the workers; estimation of the coproporphyrin content of the urine; and correlations of these with each other.

The maximum allowable concentrations (MAC) vary in different countries and in the hands of different observers. For air, the American value is given as 0·15 mgm. per cu.m.; for Russia as 0·01, and for Japan as 0·05 mgm. per cu.m. For urine, the levels vary from 0·1 to 0·2 mgm. per litre; for blood, from 50 to 100 μgm. per 100 gm.; for coproporphyrin in urine the suggested level is 0·6 mgm. per litre.

A special value for the average air concentration (*Durchschnittliche Arbeitsplatzkonzentration*—DAK) is calculated from a formula devised by the author and based on the relation between the values actually present at the time of sampling and the average time of exposure. The numerous methods at present in use for determination of all these values are described in great detail, with full particulars of reagents, apparatus and calculations. The methods chosen by the author are, for air, the dithizone process in 2 versions, a complete process designed to exclude the effect of other metals present and a shorter procedure when no bismuth and only small amounts of other elements are known to be present. For urine, the "rapid screening" method introduced by CHOLAK *et al.* [this *Bulletin*, 1948, v. 23, (260); *J. Indust. Hyg. & Toxicol*, 1948, v. 30, 59] is used, with the addition of butanol. For blood, a "wet oxidation" method uses citrated blood with the addition of HCl. For porphyrinuria, sodium carbonate and ethyl acetate are added to the specimen of fresh urine. The final estimation of all these values is made by spectrophotometry.

Investigation of the atmospheric levels of lead in the different groups of factories showed that in the accumulator works the MAC was greatly exceeded in most of the work-places; the concentration varied considerably with the time of day, rising rapidly during the morning, falling to the tolerance level during the mid-day break, and rising to a high maximum towards closing time. In the colour factories the highest concentrations—up to 10 times the MAC—were found during the preparation of dry lead oxide. In the machine shop the highest air concentrations (up to 7·7 mgm. per cu.m. in the electric welding process) were present in the cutting and welding of steel plates painted with lead paint. Good correlation existed between the accepted tolerance levels for lead in blood and urine and that of 0·15 mgm. per cu.m. in air, and with a urinary coproporphyrin level of 0·6 mgm. per litre.

In estimating the lead hazard in a particular workplace from the air concentrations, the most suitable position for taking the air samples is at the level of the head of the workers.

A full bibliography of 205 references, the majority relating to the methods of estimation described, is appended.

[For exact details of the numerous analytical methods the original publication should be consulted; the complex technicalities are not suitable for abstraction.]

Ethel Browning

SANO, S. **Studies on the Nature of the Basophilic Stippled Cells in Lead Poisoning. Report 1. Studies on the Cytological Investigation of Basophilic Stippled Cells.** *Acta Scholae Med. Univ. in Kioto.* 1958, v. 35, No. 2, 149–57, 2 figs. [25 refs.] **Report 2. Studies on the Mechanism of Granule-Formation of Basophilic Stippled Cells in Lead Poisoning.** *Ibid.*, 158–63. 1 text fig. & 7 figs. on pl. [14 refs.]

1. "In the cytological examination of basophilic stippling in lead poisoning, the author obtained the following results.

"1) The basophilic granule contains ribonucleic acid, suggesting it to be the residue of a cytoplasmic component of the erythroblast.

"2) As the granule is devoid of desoxyribonucleic acid, it is probably not derived from the nucleus of the erythroblast.

"3) The basophilic stippled cell, polychromatophilic cell and reticulocytes all contain ribonucleic acid, and in this respect the substances which characterize these cells may be considered to be identical."

2. "Continuing the studies previously reported, describing the presence of ribonucleic acid in the basophilic granule in lead poisoning, the author investigated as to whether or not the basophilic granule was already made in vivo and the mechanism of its formation.

"Using the phase contrast microscope the author made observation on the basophilic granule of the bone marrow and the peripheral blood cells in lead poisoned mice.

"1) The mitochondria were seen in the red blood cell of both the bone marrow and the peripheral blood in lead poisoning.

"2) The number of red blood cells containing mitochondria nearly approximated that of basophilic stippled cells.

"3) The vacuoles were observed in the cytoplasma of the erythroblast and red blood cell with basophilic stippling.

"4) The stippling is due to a vital aggregation of ribonucleic acid around mitochondria in the cytoplasm of red blood cell."

DAVID, A. Das Knochenmark bei gewerblicher Bleivergiftung. [**The Bone Marrow in Industrial Lead Poisoning**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 3, 329–38, 12 figs. [Numerous refs.]

Examination, haematological and cytochemical, was made of the bone marrow of 35 persons with chronic lead poisoning, and the effect upon it of administration of calcium versenate.

The bone marrow was generally hyperplastic, with increased erythropoiesis. In a few cases, where the poisoning was subacute, after short exposure, this increase was present without a correspondingly high degree of anaemia. The "shift to the left" (predominance of erythroblasts) was definite only in those with long exposure.

Mitotic activity of the erythrocytes, though higher than normal, represented an apparent increase owing to a delay in maturity since it was present only in the basophilic erythroblasts which were themselves increased in number.

Morphological changes consisted of a high degree of basophilic stippling of erythroblasts, atypical formation of the nuclei (karyorrhexis, deformation, polyploidy), presence of paraerythroblasts, variation of cell size and deficient haemoglobin content.

Siderocytes and reticuloendothelial sideroblasts, present in numbers considerably above the normal, contained an abnormally large amount of iron, indicating disturbance of the iron metabolism of these cells; the plasma frequently showed discrete basophil stippling.

Intravenous injection of 3 gm. of calcium versenate was followed by a complete return to normal in 4 of 7 persons; in the remaining 3, where severe symptoms had necessitated a higher dosage, sternal biopsy showed a hypoplastic marrow, which the author attributes to a possible inhibitory effect of the versenate on the bone marrow.

He concludes that these findings support the hypothesis that lead anaemia is initially dyshaemopoietic and subsequently haemolytic. The cellular increase in the bone marrow is due to delay in maturation; the morphological changes denote disturbance of the relation between nucleus and plasma and of haemoglobin formation; the increased phagocytic activity a haemolytic action. The apparent depression of the bone marrow in a few cases after calcium versenate therapy indicates that care should be taken in its administration.

While these changes are not specific to lead anaemia they are a useful aid to the differential diagnosis from other complex haematological disorders.

Ethel Browning

NAKASE, C. **Experimental Production of Liver Cirrhosis by Prolonged Administration of Beryllium Sulfate.** *Tokushima J. Exper. Med.* 1958, Dec., v. 5, No. 3, 171–99, 24 figs. on 3 pls. [56 refs.]

The inferior vena cava of 27 rabbits was partially occluded by ligation in order to produce congestion of the liver. Varying doses of 3% and 1% solutions of beryllium sulphate were injected into the ear veins. The injections were repeated once or twice per week up to a maximum of 24 injections. The livers were examined after death. The 4 rabbits receiving the 3% beryllium sulphate solution died within 3 days. There was widespread fatty degeneration and necrotic areas in the liver. Rabbits receiving 40–60 mgm. of beryllium sulphate in 15 to 25 divided doses survived 100 to 160 days. Their livers showed the formation of a Laennec type of liver cirrhosis. Intermediate doses produced various changes which are described and illustrated with 24 photomicrographs.

C. H. Wood

LEWIS, C. E. **The Biological Effects of Vanadium. II. The Signs and Symptoms of Occupational Vanadium Exposure.** *Arch. Indust. Health.* Chicago. 1959, May, v. 19, No. 5, 497–503, 1 fig. on pl.

The author describes a study on 24 American men who had worked for at least 6 months milling and handling vanadium. The air content of the metal at working sites was between 0·1 and 0·3 mgm. per cubic metre.

Symptoms that were significantly more common among those exposed to vanadium than among the controls included cough, irritation of nose, eyes and throat, and to a lesser extent wheezing and sputum. 37·5% of those exposed had a green tongue, 20·8% had rales or ronchi on auscultation and in 41·5% the pharynx was injected.

There was a significant increase in the concentration of vanadium found in the urine of those exposed, and the serum cholesterol levels were significantly lower.

[For Part I, see this *Bulletin*, 1959, v. 34, 910.]

T. O. Garland

BIRNMEYER, G. Inhalationsnoxen und ortsfremdes Plattenepithel im Larynx. [**Inhalation of Noxious Substances and Misplaced Localization of Squamous Epithelium in the Larynx**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 3, 294–315, 4 figs. [Numerous refs.]

After mature age, changes in the laryngeal mucous membrane are regressive, with thinning of the epithelium and transformation of ciliated into squamous cells. The object of the present investigation was to determine whether the metaplastic change from undifferentiated basal cells to squamous is chiefly due to age and constitution or is a response to the exogenous factor of inhaled toxins.

With the exception of the vocal cords and epiglottis, where primary squamous epithelium and papillae are present, the inner surface of the larynx is covered with cylindrical epithelium, extending into the deeper respiratory passages and becoming squamous at the upper border of the larynx. Cylindrical epithelium is never transformed directly into squamous by exogenous factors; when ciliated epithelium is destroyed by acute injury, the effect is made good by regeneration of a metaplastic epithelium, but the effect of prolonged and

continuous inhalation of injurious substances differs from this process chiefly in its non-physiological localization.

Particles which may enter the respiratory tissues consist of organic or inorganic mists or dusts and the so-called aeroplankton; these exert either a purely chemical, purely physical or mixed effect, and their deposition takes place first in the anterior section of the vocal cords, extending finally to the whole laryngeal mucous membrane. Although non-occupational inhalation of injurious substances is slight compared with that of workers in a contaminated atmosphere, there are non-occupational factors, such as tobacco smoke, which are not always recognized.

Histological examination was made of the epithelium of 70 specimens of larynx of human beings whose former occupational history and habits, especially that of smoking, were known. Invasion of the whole vocal cord by squamous epithelium, extending into the hypoglossal mucous membrane, was most marked in one man who had been exposed to cement dust, while among those who had a history of even heavy smoking, provided that they did not inhale, the epithelial variations were slight.

The author believes that the non-physiological location of squamous epithelium in the larynx is due to inhalation of those chemical substances whose action is intensive enough to cause lasting injury of the epithelial cells; that those inhaled toxins which have no chemically effective components play only a subordinate part, and that a combination of these exerts a summation effect. He concludes also that there is probably no direct connexion between these epithelial changes and age or sex, and that only a knowledge of the individual's habits and inhalation exposures can help to solve the problem of the aetiology of this localized occurrence of squamous epithelium in the larynx.

Ethel Browning

SHIRAKAWA, M. **Experimental Studies on the Toxicity of Benzene Hexachloride (BHC). IV. Effects of Lindane Vapor to Insects and Mammals.** *Kurume Med. J.* 1958, v. 5, No. 4, 230–44, 2 text figs. & 12 figs. on 2 p!s. [24 refs.]

Groups of 2–5 male and female rats were exposed daily (6 days each week) for 1 hour or 5 hours for up to 127 days to lindane. 0·1, 1·0 and 10 gm. of lindane were heated over a 100-watt lamp in a 1 m.^{3} chamber in which the animals were exposed. Atmospheric concentrations were not measured.

Exposure to 10 gm. killed the rats in a few days. Exposure for 5 hours to 1 gm. produced signs of irritation and the rats died within 106 days. Rats exposed to 0·1 gm. survived for 127 days and showed some evidences of lung injury.

Insects (*Sarcophaga*) exposed to 0·1 or 1 gm. were affected within 10–15 minutes and died within a few hours.

[For earlier parts, see this *Bulletin*, 1959, v. 34, 353.]

J. M. Barnes

GABOR, Silvia. Modificazioni degli enzimi nel benzolismo [**Enzyme Changes in Benzolism**] *Med. d. Lavoro.* 1959, Apr., v. 50, No. 4, 257–63, 5 graphs.

The biochemistry of chronic benzolism is still incomplete so this paper from the Institute of Hygiene at Cluj (Rumania) is of interest.

Gabor points out that benzolism is a disturbance of oxidation-reduction so the effects were tested of chronic benzolism on 3 blood enzymes: peroxidase, catalase, and indophenoloxidase.

Tests were carried out on adult white rats, 25 being poisoned with varying concentrations of benzol; 37 acted as controls. The rats were exposed for 3 hours a day on alternate days, first, to a concentration of 0·1 mgm./litre for 130 days, then to 1·0 mgm./litre for 28 days, and finally to 2·5 mgm./litre for 7 days.

The results were: Peroxidase: for 126 days values gradually rose to 30% above normal, then fell abruptly; Catalase: this decreased with the increase in peroxidase, but when higher concentrations than 0·1 mgm./litre were given it fell to below 50% of the control values; Indophenoloxidase: in the lowest concentration values were about normal, but with increased concentrations values declined continually.

Gabor considers that early evidence of disturbance of oxidation-reduction is the change in catalase-peroxidase ratio—increased peroxidase with reduced catalase —even in concentrations of 0·1 mgm./litre for a long period. With increased concentrations the reduced peroxidase is *not* accompanied by increased catalase, which indicates an exhaustion of the defence mechanisms. This merits attention since it may represent the passage from functional disturbances to morphological lesions. The author finally mentions that these enzyme changes appeared rather later than certain central and peripheral nervous changes seen in the same group of animals.

The blood cytology did not show the changes characteristic of chronic benzolism.

W. K. Dunscombe

BARTONÍCEK, V. & SOUCEK, B. Der Metabolismus des Trichloräthylens beim Kaninchen. [**The Metabolism of Trichloroethylene in Rabbits**] *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 3, 283–93, 2 figs. [16 refs.]

This investigation was undertaken with a view to estimating the metabolic behaviour of trichloroethylene, its excretory products, trichloroethanol and trichloracetic acid, the percentage of retained trichloroethylene, the rapidity of saturation and desaturation, the tolerance for trichloroethylene by parenteral administration and the dependence upon diuresis of the urinary excretion of the metabolites.

Only 6 animals were used and the method of administration (intramuscular injection of 1 ml. of trichloroethylene in 2 ml. olive oil) though not corresponding to chronic poisoning in human beings from inhalation, was chosen chiefly on account of its simplicity. The injections were given every 2 days for a period of 45 days, and followed by a period when none was given, during which the urinary estimations were carried out.

The animals lost, on average, 25% of their weight, and 3 died, 2 with symptoms of kidney injury. Albuminuria was present in the animals which succumbed after 55, 71 and 91 days, but not in the 3 survivors, whose urine reduced Fehling's solution, suggesting the excretion of trichloroethanol gluconide.

The amount of trichloracetic acid excreted in the urine was about 0·3% of the retained trichloroethylene (about 50 times less than with human beings) and of trichloroethanol about 45% (average for human beings 50%). Comparing the relative amounts of these substances excreted by animals with that by human beings, it appeared that animals excreted 1·8 times more trichloroethanol and 50 times less trichloracetic acid. The maximum amount of trichloracetic acid was excreted on the third day after the beginning of the experiment and it was present in the urine 14 days after the injections ceased—a slow excretion similar to that observed in human beings. One-half of the trichloroethanol was excreted in about 20 hours, its highest concentration being present almost immediately after injection. It is concluded that the metabolism of trichloroethylene in animals is qualitatively, but not quantitatively, identical with that of man. From these experiments it was not found possible to state which metabolite is responsible for the toxicity of trichloroethylene. *Ethel Browning*

Sziza, M. & Magos, L. Toxikologische Untersuchung einiger in der ungarischen Industrie zur Anwendung gelangenden aromatischer Nitroverbindungen. **[Toxicological Investigation of Some Aromatic Nitrocompounds used in Industry in Hungary]** *Arch. f. Gewerbepath. u. Gewerbehyg.* 1959, v. 17, No. 3, 217–26, 1 fig.

The aromatic nitro compounds under examination included nitrobenzene, p-nitrochlorobenzene, 2.4 dinitrochlorobenzene, p-nitroanisol and p-nitrophenetol. These were administered to white rats by mouth, intraperitoneally, and percutaneously in a 10% aqueous gum-resin suspension. After 14 days the various organs and tissues were examined histologically, and the haemoglobin and methaemoglobin content of the blood estimated. The irritative effect on the skin was examined by percutaneous injection of dilute solutions in acetone, and on the eyes by application to the cornea of the finely powdered substance.

On the basis of the LD50 values suggested by Hodge and Sterner in 1947 p-nitrochlorobenzene, with a figure of 3, was the most toxic, and p-nitrophenetol, with a figure of 6, the least.

With nitrobenzene as the basis for comparison of toxicity, it was found that p-nitrochlorobenzene is more toxic by intraperitoneal and oral administration, but one-tenth as toxic by percutaneous. The highest intraperitoneal toxicity was shown by 2.4 dinitrochlorobenzene, p-nitrophenetol was non-toxic by the percutaneous and oral routes, and p-nitroanisol by percutaneous, but both were almost as toxic as nitrobenzene by intraperitoneal injection.

With regard to formation of methaemoglobin, the most toxic compound was 2.4 dinitrochlorobenzene, and p-nitrochlorobenzene was more toxic than nitrobenzene. These 3 compounds produced intensive formation of Heinz bodies, in contrast to p-nitrophenetol.

The strongest irritative effect on the eyes was exerted by 2.4 dinitrochlorobenzene, followed by p-nitrochlorobenzene, p-nitroanisol and nitrobenzene; p-nitrophenetol was practically non-irritant.

Skin irritation and sensitization was observed only with 2.4 dinitrochlorobenzene.

The histological variations differed little with any of the compounds; the liver and kidney injuries observed —parenchymatous and fatty degeneration—were not considered specific. *Ethel Browning*

Walworth, H. T. & Virchow, W. E. **Industrial Hygiene Experiences with Toluene Diisocyanate.** *Amer. Indust. Hyg. Ass. J.* 1959. June, v. 20, No. 3, 205–10, 6 figs.

Among the basic ingredients for the manufacture of polyurethane foam slabs and moulded products are combinations of toluene 2,4-diisocyanate and toluene 2,6-diisocyanate (TDI), polyester or polyether resins and catalysts. Foaming starts and may end quickly; mixing and curing are necessary; unreacted and uncured chemicals may accumulate; the reaction is exothermic, with liberation of CO_2: these conditions may cause pollution with TDI though its vapour pressure is low and boiling point as high as 247°C.

During continuous production of thick slabs, 48 inches wide, the nozzle of the machine mixer deposits a thin layer of liquid which foams, according to adjustments, to a height of 12 to 16 inches on the conveyer belt inside a machine, 40 feet long open only at the ends. The slab is usually cut into 6-foot lengths and oven-cured or stacked. Moulded products operations were improved: eventually an automatically measured prepolymer liquid was treated by the catalyst only just before manual cup-mixing and pouring.

Production started early in 1955 but it was not until the cool weather that complaints and absenteeism became a problem and a case of asthma was tentatively associated with the polyurethane processes. Studies of exposure to TDI began in October. In 17 months over 1,000 air samples were analysed, there were changes in processes and equipment and TDI concentrations gradually decreased. During this period 83 cases of respiratory illness were related to exposure among a population which numbered about 200 during the first winter, was less until autumn 1956, and rose to 350 or 400 during the following winter. In the next 15 months there were 16 cases of illness among this larger population, which however decreased again until autumn 1957 and then returned to 400. The illness appeared 3–4 weeks after exposure to TDI, workers once affected could not tolerate any re-exposure, but there was no direct correlation between degree of exposure and respiratory symptoms. This was possibly due to individual sensitivity, brief accidental exposure to relatively high concentrations not indicated by the integrating sampling method and inadequate sickness records.

The highest TDI vapour concentration detected was

2·2 p.p.m. in March 1956 in the pouring area. Average general monthly concentrations ranged from about 0·15 p.p.m. in 1955 to 0·05 p.p.m. and less throughout 1957. This field study tends to support the need for a very low exposure limit. *M. Patricia Fitzsimons*

CROTON, L. M. **Carbon Monoxide Poisoning—a Current Controversy.** *J. Inst. Sci. Technol.* London. 1959, Apr.–June, v. 5, No. 2, 20–23, 1 fig. [14 refs.]

In 1938 Cecil K. DRINKER published figures showing that deaths among those treated for carbon monoxide poisoning had declined dramatically in New York since a 7% CO_2 + 93% O_2 mixture had been used for treatment of gassed persons instead of pure oxygen (*Carbon Monoxide Asphyxia*, 1938, New York, Oxford University Press.

A report by the Medical Research Council in 1955 had concluded that carbon dioxide should *not* be administered at all with oxygen in any case requiring resuscitation on account of asphyxia. Subsequently this conclusion was challenged by H. L. MARRIOTT and the MRC set up a special sub-committee to review all available evidence on the matter. This committee recommended 5% CO_2 + 95% oxygen for the treatment of asphyxia from carbon monoxide poisoning only—a recommendation that was once more challenged by Marriott, who wishes the 7% CO_2 + 93%O_2 mixture to be used. His challenge is a strong one [this *Bulletin*, 1959, v. 34, 789].

The most encouraging note now comes from *Hansard* (13 February 1959) where it is reported that the gas industry is working on a process to produce coal gas with little or no content of carbon monoxide. At present for every 3 fatalities in Great Britain from road accidents there are 2 deaths from carbon monoxide poisoning, so this controversy is no mere academic exercise. *T. O. Garland*

WOLFSIE, J. H. & SHAFFER, C. B. **Hydrogen Cyanide. Hazards, Toxicology, Prevention and Management of Poisoning.** *J. Occupational Med.* Chicago. 1959, May, v. 1, No. 5, 281–8. [41 refs.]

The toxicological and medical parts of this up-to-date review can be applied to inorganic cyanides since the poisoning is a function of the cyanide ion, one of the most powerful and rapid poisons known and yet seldom fatal in industry because treatment by the amyl-nitrite—sodium-nitrite—sodium-thiosulphate method is effective. This calls for forethought, equipment ready to use, organization and training, and the details are well documented. [See also this *Bulletin*, 1950, v. 25, 1269.]

HCN, liquid or vapour, is volatile. Stable anhydrous HCN under certain influences may undergo decomposition and polymerization and the colourless liquid may darken. Explosive violence may develop. The reactivity of the chemical makes possible specific and sensitive methods of detection. Though some people can detect 1 p.p.m. by odour, the danger from inhalation demands that chemical detectors should be used and understood. The MAC of HCN vapour is 10 p.p.m. by volume for an 8-hour day. Neither liquid nor vapour is irritating and both are rapidly absorbed through alveolar and intestinal epithelium—and particularly the liquid, through the skin; diffusion is rapid.

CN poisoning results in cellular anoxia, with corresponding symptoms. The characteristic odour has hardly ever been detected in the breath after inhalation poisoning. Cyanosis has not been an important sign, probably because of rapid treatment. The toxicological action is made clear from the two-fold basis of treatment: promotion of the activity of the transsulphurase system to effect a more rapid conversion of CN to the relatively non-toxic thiocyanate; and induction of methaemoglobinaemia in order that a substance containing ferric iron is made available to combine with CN which would otherwise inactivate cytochrome oxidase. The toxic action of CN depends on its ability to form complexes with metal ions and is manifested in disturbances of various enzyme systems, particularly the heme-porphyrin complexes containing trivalent iron. Haemoglobin, containing ferrous iron, is relatively unaffected. The union of CN with ferric iron complexes is reversible, if death does not intervene, and the CN is eventually disposed of by the transsulphurase mechanism and renal excretion of thiocyanate. Symptoms which have been attributed to chronic CN poisoning on environmental circumstantial evidence are identical with those of thiocyanate intoxication; in detoxifying absorbed CN it is possible that the person who is regularly exposed to HCN may accumulate thiocyanate in the extracellular fluids.

Specific treatment—in addition to removal from exposure, artificial respiration and decontamination—starts with administration of amyl nitrite by inhalation, 5 minims (0·3 ml.), repeated if necessary every 5 minutes for 25 minutes. If there is no response a doctor injects intravenously 10 ml. of a 3% solution of sodium nitrite at a rate of 2·5–5 ml. per minute and then, similarly, 50 ml. of a 25% solution of sodium thiosulphate; this is repeated in half doses in 2 hours or in 1 hour if signs persist or recur. Oxygen has not been necessary, though the induced methaemoglobinaemia may cause anoxaemia severe enough to need it. Marked fall in blood pressure from the nitrite may need epinephrine or ephedrine. Recovery can be expected as long as the heart is beating and will be complete unless complete anoxia had been prolonged.
M. Patricia Fitzsimons

BALGAIRIES, E. & CLAEYS, C. L'examen toxicologique des atmosphères des ateliers de fabrication des résines synthétiques. [**Atmospheric Investigation for Toxic Substances in Synthetic Resin Production Workrooms**] *Arch. Malad. Professionnelles.* Paris. 1959, May–June v. 20, No. 3, 312–14.

This communication outlines the method by which effective atmospheric control was maintained for 3 years without the occurrence of acute or chronic poisoning. Toxic compounds were used and an unpredictable mixture of contaminants could diffuse during manufacture of copolymer resins. Atmospheric sampling was carried out regularly and the samples were examined by infra-red spectrophotometry. Because many compounds were unreactive chemical analysis

could not be specific or sufficiently sensitive, and gas chromatography was ruled out because of the dusts.

Sampling was carried out systematically in 2 ways: into a vacuum flask direct and into mixers, containing a solvent, by means of a mobile unit which pumped a measured, large volume of air. The solvent depended on the main constituents of the resins. As a rule 2 samples were collected for bubbling through a solvent, 1 into a mixer, supplied with a heater, containing purified redistilled cyclohexane, and another into repurified absolute alcohol.

The vacuum flask sample was examined immediately by reflection in a long column and this gave as a start an indication of the group of any organic impurities in gas or vapour form. When necessary, the spectrum in a 10 cm. tube was compared with standards to determine the composition. The dissolved samples were evaporated at low temperature under nitrogen at about 40 mm. Hg, and the residues, which were generally syrupy, were examined by direct infra-red spectrophotometry in a sodium chloride cell, 0·025 mm. thick. By this examination contaminants in liquid or solid form were determined. Not all possible toxic substances would be uncovered, but the only mineral catalyst, boron fluoride, was tested for separately.

Immediately a sample showed the presence of any contaminant, generally only as a trace, a systematic search was made for leaks in the production circuits which were usually responsible. The authors believe that there is hardly any general solution of the problems of this type of contamination except one such as they use, or one based on the same principle though possibly with a different analytical method.

M. Patricia Fitzsimons

HEALY, J. K. **Ascending Paralysis following Malathion Intoxication: a Case Report.** *Med. J. Australia.* 1959, June 6, v. 1, No. 23, 765–7. [18 refs.]

A short review of some of the literature on the toxicology of organic phosphate insecticides introduces a report of a case of poisoning by malathion in a boy aged 18 months: The case is of interest for the following reasons—(1) "poisoning by malathion is less common than is poisoning with other readily available members of the group", (2) an ascending paralysis developed some weeks after the acute symptoms appeared and this has not previously been observed after malathion poisoning, and (3) hypertension and glycosuria developed and these had interesting characteristics.

During the 6 weeks before admission to hospital the boy was exposed daily to malathion which was used as a garden spray. In addition to the amount absorbed through the skin and by inhalation, some malathion was also ingested by eating buds of plants which had been sprayed. Soon after spraying began the child became irritable and lost appetite. Within a week he was feverish. After 6 weeks he had lost 7 pounds in weight, had developed polydipsia and was seen to drag his legs when walking and to fall over easily.

His clinical condition on admission to hospital is described. In the next few days his state progressed to a complete flaccid paralysis of the lower limbs which then spread to the trunk and upper limbs. He remained febrile, anorexic and irritable. The systolic blood pressure was 210 mm. of mercury. Therapy by hypodermic doses of atropine given every 3 hours (1·2 to 2·4 mgm. daily) was then begun and continued for some weeks at a daily dosage of 1·2 mgm. without side effects. There was some immediate response to the first doses of atropine and ultimately motor power was restored. Blood pressure remained high under atropine but became normal after treatment with reserpine. The general condition returned to normal in 4 weeks. There is a discussion of the paralysis, hypertension and glycosuria.

In the conclusions it is stated that malathion can produce the acute symptoms and signs related to acetylcholinesterase inhibition, but that the paralysis does not seem to be related to this inhibition. *M. E. Delafield*

DAVIES, D. R. & GREEN, A. L. **The Chemotherapy of Poisoning by Organophosphate Anticholinesterases.** *Brit. J. Indust. Med.* 1959, Apr., v. 16, No. 2, 128–34. [66 refs.]

Poisoning of mammals by the organophosphates that inhibit cholinesterase is believed to result from the accumulation of acetylcholine. Atropine which counteracts the action of acetylcholine at certain sites has long been recognized as an effective therapeutic agent in cases of poisoning by these compounds. Atropine only counteracts the effects of an inhibition of cholinesterase. This paper traces the development of work aimed at achieving a reversal of the inhibition with a reactivation of the enzyme. By studying the ability of certain groups, notably hydroxylamines, to react with alkyl phosphates, and combining this group in a molecule containing a quaternary nitrogen an effective reactivating agent of low toxicity—pyridine-2-aldoxime methiodide—was discovered simultaneously in two laboratories. The quaternary N is believed to attach itself to the enzyme at the same site as acetylcholine and so bring the oxime into close proximity to the alkyl phosphate group attached to the esteratic site on the enzyme. On reaction taking place, the product leaves the enzyme. P2-AM,* especially if combined with atropine, has been shown to be very valuable in poisoning by certain organo-phosphorus compounds. Other compounds that react with organophosphates or reverse the inhibition are described but have various drawbacks including undesirable toxicity. Recently bis quaternary compounds resembling a double molecule of P2-AM have been shown to be more effective. The authors stress the important part played by fundamental biochemical studies in the development of these valuable therapeutic agents. *J. M. Barnes*

[*In the original paper the compound is referred to as PAM. This is most undesirable as it must lead to confusion with penicillin with aluminium monostearate, long and widely known as PAM. *Ed.*]

Atmospheric Pollution

STOCKS, P. **Cancer and Bronchitis Mortality in relation to Atmospheric Deposit and Smoke.** *Brit. Med. J.* 1959, Jan. 10, 74–9, 2 figs. [15 refs.]

Dr. Percy Stocks here presents evidence on the relationship in different areas of England and Wales of mortality in 1950–3 from bronchitis and lung and other forms of cancer to atmospheric pollution. The indices of pollution were derived from data published by the Department of Scientific and Industrial Research. The "deposit index" is the number of grammes of undissolved matter deposited on 100 square metres of surface per month. The "smoke index" is derived by drawing a measured volume of air through a white filter paper and matching the darkness of the stain against a standard scale. Mortality from each cause is expressed as a standardized mortality ratio for each sex or for both sexes combined. This is 100 times the ratio of observed deaths in an area to those expected in the same population at the age-sex-specific death-rates of England and Wales.

In those county boroughs having the necessary pollution data, bronchitis mortality was very significantly correlated in each sex with both deposit and smoke, when the effect of population density was eliminated. The same relationships held for lung cancer, in both sexes together, and for stomach cancer with smoke in females. The other correlation coefficients of stomach cancer with air pollution in county boroughs (males with both indices, and females with deposit) reached a significance between 5% and 1%.

In administrative areas of Lancashire and Yorkshire having the necessary pollution data, bronchitis mortality was again found to be very significantly related to deposit. Lung cancer deaths were not related to deposit. They were significantly related, but not highly so, to smoke, while bronchitis deaths on the other hand showed no significant relationship to smoke in these areas. Female, but not male, stomach cancer deaths were just significantly related in the same areas both to smoke and to deposit.

In the urban areas of Lancashire, and also in all areas of this county, lung cancer deaths were independently correlated with the population density of the surrounding districts, even when that of the town or area itself was held constant. Higher correlation coefficients were found between lung cancer mortality and an index obtained from a weighted average of the population density of each area and half that of the surrounding areas, than between lung cancer mortality and the population density of the area itself, or between such mortality and the surrounding districts alone. Dr. Stocks considers that these results appear to confirm the effect of wind-borne smoke upon the incidence of the disease. The relationship of stomach cancer mortality to deposit and to smoke may in his opinion be due to the exposure of food to polluted air. In the United States, where food is more extensively wrapped than in Britain, deaths from this disease have been steadily falling in recent years.

A. S. Fairbairn

SMITH, R. G., MACEWEN, J. D. & BARROW, R. E. **The Occurrence of Phenols in Air and Combustion Products.** *Amer. Indust. Hyg. Ass. J.* 1959, Apr., v. 20, No. 2, 149–52, 2 figs.

"Public concern with the causes and effects of air pollution has resulted in increasing scientific interest in the nature of the chemical mixture present in the atmosphere." Nevertheless, although "enormous amounts of information are already available" knowledge on specific subjects is inadequate. This is the case with the pollution of air by phenols, a subject which the authors of this paper have accordingly studied. The methods of study, complete details of which were given in a previous publication (*Amer. Indust. Hyg. Ass. J.*, 1959, v. 20, 142), consisted of collecting samples of particulate matter and of vapour and analysing these by a modification of the 4-amino-antipyrine procedure for phenols in water with confirmation of the presence of phenols in the samples in some instances by ultra-violet spectrophotometry.

The results of these analyses are described, discussed and set out in tables. The main site at which samples of city air were taken was on the roof, 9 storeys up, of a university building, Detroit. Several hundred samples of air were taken over a period of more than a year and the mean concentration of phenols was, in μgm. per cubic metre, 0·0693 for particulate matter and 4·29 for vapour. Limited numbers of samples of air from other locations were also taken and gave the mean results for total phenols 19·0 μgm./m.^{3} in a street with moderate traffic, 20·3 in a heavy chemical industrial area and 566 in a phenol-emitting plant area. A limited study was also made of phenols in combustion products and the mean results obtained were 13·1 μgm. for domestic oil furnaces, 37·7 for domestic gas furnaces and the very high figure of 13,600 μgm./m.^{3} for idling automobile exhaust.

Studies are in progress to identify the specific compounds present in air and exhaust products.

M. E. Delafield

GRANDJEAN, E. Untersuchungen über die Wirkung von Zementstaub-Verunreinigung der Aussenluft auf die Gesundheit ortsansässiger Bevölkerungen. [**Investigations of the Effect of Cement Dust in the Air on the Health of the Population of the Neighbourhood**] 8 pp., 6 figs. [? 1958.] Zurich: Inst. f. Hyg. u. Arbeitsphysiol. der Eidgenössischen Technischen Hochschule.

The study described in this paper was undertaken in order to compare the frequency of illnesses in the general population in 2 districts in Switzerland in which there are cement factories with that of the population in 4 villages not so exposed to cement dust in the atmosphere. As introduction some of the literature on the effects of polluted atmosphere on the health of the general population and also on the occupational diseases of cement workers is quoted.

Particulars of the 2 populations which were compared are given by number and occupation, by age and sex distribution. Morbidity records were obtained from the Swiss health insurance society with which a large number of the people are insured. Figures and description set out the results of the comparative analyses of the sickness experience of the 2 populations by age, sex and nature of disease in the period 1952–6. The findings were that the general morbidity in the cement dust areas was no greater than that in the villages nor was there any significant difference in the type of disease experienced.

No accurate determinations of the dust pollution of the 2 areas have as yet been carried out. It is to be noted that the actual numbers of the insured persons from whom the morbidity records were obtained are given in tables as 311 in the 2 cement dust areas which have a total population of 2,756 and 631 among 6,293 persons in the 4 villages. *M. E. Delafield*

CRAMER, H. E. **Engineering Estimates of Atmospheric Dispersal Capacity.** *Amer. Indust. Hyg. Ass. J.* 1959, June, v. 20, No. 3, 183–9, 9 figs. [15 refs.]

Physiology as Applied to Hygiene

LINDERHOLM, H. **Diffusing Capacity of the Lungs as a Limiting Factor for Physical Working Capacity.** *Acta Med. Scandinavica.* 1959, Feb. 7, v. 163, No. 1, 61–84, 4 figs. [55 refs.]

The extent to which alveolar-capillary diffusion (D_L) can limit oxygen uptake in health and disease is not precisely known. This problem was investigated by measuring D_L at rest and at maximum work capacity (bicycle ergometer) in 12 normal persons (including 4 athletes) and 18 patients (alveolar-capillary block, 5; pneumonectomy, 6; emphysema, 4; mitral stenosis, 3).

In normal persons D_L appeared to increase with rate of work although at a slower rate when approaching maximum work output. In alveolar-capillary block D_L seemed to increase at least as much as in normal persons in relation to O_2 uptake and pulse frequency: nevertheless the rate limiting factors seemed to be diffusion and ventilation. In the pneumonectomy group, cardiac output appeared to be the limiting factor. In mitral stenosis the primary defect was also circulatory. In emphysema, ventilation was thought to be the limiting factor. *M. L. Thomson*

Sanitation

WATER AND SWIMMING BATHS

(Including the Bacteriology of Water Supplies)

MORELIS, P. & COLOBERT, L., with the technical collaboration of R. GROSJEAN and J. SERERO. Un milieu selectif permettant l'identification et le dénombrement rapides de *Streptococcus faecalis.* [**A Selective Medium for Rapid Identification and Counting of** *Streptococcus faecalis*] *Ann. Inst. Pasteur.* 1958, Nov. & Dec., v. 95, Nos. 5 & 6, 568–87; 667–80, 7 figs. [41 refs.]

The authors have tried to prepare a medium for rapid isolation and identification of *Str. faecalis* which is simple to carry out and at the same time is sensitive.

After studying 173 strains of enterococcus from human and animal stools and from other pathological material, it was concluded that the medium should be capable of isolating all biotypes of *Str. faecalis.*

The medium may be used in connexion with filtration counting procedures and incubation for 8–12 hours in semi-anaerobic conditions produces luxuriant growths of enterococcus.

The composition of the medium is as follows:—

Peptone (Vaillant 5B)	10 gm.
Glycocoll	5 gm.
Powdered agar	16 gm.
Distilled water *p*H 9·3	800 ml.
Sodium azide	2·0 gm.
Aesculin	1 gm.
Iron ammonium citrate	2 gm.
Distilled water	200 ml.

Sterilization was by autoclaving at 115°C. for 20 minutes. *E. Windle Taylor*

SUREAU, P., with the technical colloboration of R. RABESOA. Recherche et numération des streptocoques fécaux dans les eaux en utilisant les membranes filtrantes. [**Isolation and Enumeration of Faecal Streptococci in Waters by means of Filtering Membranes**] *Ann. Inst. Pasteur.* 1958, Dec., v. 95, No. 6, 768–72. [10 refs.]

The "M-Enterococcus Agar" medium proposed by SLANETZ and BARTLEY [this *Bulletin*, 1958, v. 33, 495]

has been adopted by the Pasteur Institute of Madagascar for the isolation and enumeration of faecal streptococci in water samples in association with membrane filtration technique. *E. Windle Taylor*

HENDERSON, W. L. **Studies on the Use of Membrane Filters for the Estimation of Coliform Densities in Sea Water.** *Sewage & Indust. Wastes.* Wash. 1959, Jan., v. 31, No. 1, 78–91, 4 figs. [14 refs.]

Coliform concentrations in sea water and mixtures of sewage and sea water were determined by the membrane filter method in parallel with the multiple tube fermentation test.

It was concluded that the membrane filter method has advantages over the fermentation tube method by virtue of the saving in labour, time and materials. Furthermore the results by membrane filtration are available earlier and this is advantageous from a control point of view.

The precision of the count obtained from a membrane is superior to the most probable number figure derived from a series of positive and negative tubes.

The fact that the membrane filter counts were generally lower than the most probable number counts was not considered to be due to the poorer performance of the filter method but to the fact that production of gas in the brilliant green bile broth tubes may, on occasion, be caused by non-coliform organisms. This was supported by a limited number of comparative tests on diluted broth cultures of coliform organisms in that the membrane filter count was in better agreement with the total count than was the most probable number. *E. Windle Taylor*

HEINRICH, S. & PULVERER, G. Ein Beitrag zur Methodik des *Salmonella*-Nachweises in Abwasser, Flusswasser und Schlamm. [**A Study of Methods of Isolation of Salmonella Organisms from River Water, Sewage and Mud**] *Ztschr. f. Hyg. u. Infektionskr.* 1959, v. 145, No. 6, 529–42. [28 refs.]

A simple enrichment method for determining salmonellae in sewage, river waters and mud is described which has been developed in the course of investigations on the question of eliminating these organisms from sewage through clarification. The procedure is based on using a 10 times concentrated nutrient solution and allows a relatively large yield with a proportionately small outlay of labour and materials, which makes it specially suitable for routine work.

For the quantitative estimation of the salmonella load of water or mud samples a salmonella titre can be determined by this method. *E. Windle Taylor*

DARRASSE, H., LE MINOR, L. & LECOMTE, M. Isolement de plusieurs *Salmonella* dans une eau de distribution: originalité de la contamination. [**Isolation of Salmonellae from the Dakar Water Supply; Unusual Source of Contamination**] *Bull. Soc. Path. Exot.* 1959, Jan./Feb., v. 52, No. 1, 53–60. [14 refs.]

This is an account of the isolation from the Dakar City Water Supply of salmonella sero-types, the associated investigations in tracing the source of these contaminations and a discussion of the hazards involved. The method employed for the isolation of the salmonellae from the water was the more or less standard technique of passing some 5 litres of the water under test through a Seitz EK pad fitted in a negative pressure filtration apparatus, dropping the filter-pad directly into a suitable enrichment medium and finally plating out after about 16 hours' incubation from this medium. Epidemiological studies showed that the contaminations did not come from the original water source but from a tank reservoir openly exposed to heavy contamination from the faecal droppings of lizards. Examination of the guts of a sample of these lizards showed that they harboured the same salmonella sero-types as those found in the water supplies and also in the faeces of the local population consuming the water.

H. J. Bensted

DELIUS, I. Verfahren zur Beseitigung schädlicher Nitratgehalte aus dem Trinkwasser. [**The Removal of Dangerous Concentrations of Nitrate from Water**] *Gesundheits-Ingenieur.* 1959, June 10, v. 80, No. 6, 181–5, 3 figs.

Reference to the methaemoglobinanaemia which may occur in artificially fed infants whose feeds have been made up with water of high nitrate concentration [this *Bulletin*, 1958, v. 33, 865] introduces this account of experiments undertaken to study methods for the removal of the nitrate ion. Chemical reduction of nitrate by metals—iron, aluminium or magnesium—was found not to be satisfactory. Elimination of nitrate by the addition of cultures of algae has been investigated by some workers but found to be impracticable.

Most of this paper is devoted to an account of experiments on the use of the method of ionic exchange. The material used was a strongly basic anionic exchange product (ES made by Permutit AG, Berlin). Sulphate, chloride or carbonate anions were introduced by treatment of ES with the sodium salts or these anions followed by thorough washing. Water from the Berlin supply to which potassium nitrate was added to bring the concentration of NO_3 to 100 mgm. per litre was then filtered through each of the 3 anionic exchange materials. The nitrate ion was removed by all 3 but the efficiency of exchange was greater by the chloride ion and the bicarbonate ion than by the sulphate ion material. It was found, for example, in filtration experiments with the chloride-ion material that 50 gm. of this removed all the nitrate from over 24 litres of the water. Full numerical details of the results are set out in tables with a discussion.

M. E. Delafield

PUBLIC HEALTH REP. Wash. 1959, June, v. 74, No. 6, 511–20. **Fluoridation. 1. Statement by A. S. Flemming** (Sec. Health, Education, & Welfare), 511–13. **2. Report on Fluoridation in the United States,** 513–16, 1 chart. **3. Statements on Proposed Alternatives to Fluoridation of Water Supplies,** 517–20.

1. In the U.S.A. there has been during the past 2 years a set back in the progress of controlled water

fluoridation. Flemming finds it difficult to understand why this should be so in the light of the known facts regarding the benefits of fluoridation, and he concludes that the opponents of fluoridation are a militant minority, while the proponents are an unmilitant majority. He respects those who oppose fluoridation as a matter of principle, but the most vocal opponents are persons who have been charged by the Food and Drug Administration with making false health claims for nostrums and other devices which influence their customers against seeking needed medical advice.

2. The U.S. Division of Dental Public Health records that today more than 42 million people in the U.S.A. are drinking water containing the minimum or higher level of fluoride recommended. Of these, 35 million live in communities where the fluoride concentration in the water is controlled, and 7 million use water naturally containing 0·7 p.p.m. or more fluoride. It is disconcerting to find, however, that there has been a steady decline in the rate of community acceptance in the past 6 years. The peak year for fluoridation was 1953, during which 378 communities adopted fluoridation, whereas only 145 began fluoridation programmes in 1958. Moreover, the number of communities which discontinued fluoridation programmes in the past 5 years has steadily increased.

3. The pros and cons of administering fluoride in vehicles other than water supplies are discussed. Sodium fluoride tablets have been tried, but doubts are expressed regarding the maintenance of a daily constancy of purpose on the part of the mother. The cost of bottled water fluoridation would be prohibitive. Fluoridation of milk is not practicable when there are very wide variations in the amount of milk drunk by different children. As for bread, it is probable that not much would be eaten in infancy during the early stage of tooth development. Salt is another possible vehicle, but there is no exact information regarding its consumption by different age-groups.

Robert Weaver

SEWAGE, TRADE WASTE AND REFUSE DISPOSAL

MINISTRY OF HOUSING & LOCAL GOVERNMENT. **Second Progress Report of the Standing Technical Committee on Synthetic Detergents** [CREMER, H. W., Chairman]. 10 pp. 1959. London: H.M. Stationery Office. [9d.]

In January 1957 the Ministry of Housing and Local Government appointed a Standing Technical Committee to keep under review the difficulties in sewage and water treatment resulting from the use of synthetic detergents. The first progress report was issued in October 1957; the second was published recently.

In the first report estimates were given to show that the concentration of these surface-active materials that might be expected in sewage or in rivers was unlikely to increase. This prognosis has been borne out by the regular analyses made by a number of River Boards, Water Undertakers and Sewage Authorities.

The Committee seems to be hopeful of the results to be expected from the production of new detergent materials, among which are straight chain alkylbenzene-sulphonates and the sucrose esters. Both kinds of material are at present being examined.

Work on the pilot scale, both with biological filters and with activated sludge, at the Water Pollution Research Laboratory showed that 94% of the new alkylbenzene-sulphonates can readily be removed. With the average concentration now experienced in settled sewage in 17 different sewage works in England, namely 13 p.p.m., this will leave a residual concentration of less than 1 p.p.m.

An investigation carried out at Gunthorp Weir on the River Trent showed that river water contained about 1 p.p.m. of anionic surface-active material and that the wet foam contained 1,200 p.p.m.; and that when this was evaporated down, 40% of the dry matter was found to consist of anionic detergent. Results of a number of analyses of foam collected from various works suggest that the concentration of detergent in the foam is not greatly affected by the concentration in the liquid from which the foam is produced. The Water Pollution Research Laboratory finds the tendency to produce foam is greatest in clean water, becoming progressively less as the water becomes dirtier.

The London County Council is investigating the removal of surface-active material in the form of foam by intensified aeration of the influent to an activated-sludge plant.

Toxicity experiments on fish show that concentrations of these materials likely to be present in British rivers are unlikely to have a directly toxic effect on fish.

Peter C. G. Isaac

KELLY, Sally & SANDERSON, W. W. **The Effect of Sewage Treatment on Viruses.** *Sewage & Indust. Wastes.* Wash. 1959, June, v. 31, No. 6, 683–9, 1 fig. [16 refs.]

Knowledge of the destruction of viruses by sewage treatment is limited to laboratory observations and to a very few treatment plant studies. The work described in this paper was undertaken to determine the types of sewage treatment that destroy viruses under full-scale conditions in the United States.

Samples were obtained by the swab method in flowing sewage and over 140 samples of raw and treated sewage were examined. Over 166 strains of virus were isolated, including poliomyelitis, Coxsackie groups A and B and ECHO types. Isolations were made with all the well-known hosts, namely, newborn mice, monkey kidney epithelium, human amnion tissue and He La cells.

In summer months some 80% of samples of raw sewage contained viruses, but this frequency fell to 10% in the winter.

Primary sedimentation of sewage did not remove the viruses but there was a reduction in the total number of infectious particles; probably by removing the viruses in the settleable solids. Similarly secondary treatment

on percolating filters did not remove viruses completely, but the density of concentration was probably reduced by some 40%. Effluents from secondary treatment plants that had been chlorinated still contained viruses in one-third of the samples. Residual chlorine values of 0·5 p.p.m. were obtained and it was shown that disinfection had some destructive effect, because plaque counts were lower in chlorinated effluents than in the untreated liquid.

A few samples of activated sludge effluent and of Imhoff tank sludge and digested sludge were examined and viruses could not be isolated from them.

Laboratory studies of the effect of large doses of chlorine indicated that, depending on *p*H and temperature, residual combined chlorine values of 9 p.p.m. and greater with 15 minutes' contact or of 0·5 p.p.m. with 4 hours' contact were necessary for inactivation of viruses. *E. Windle Taylor*

Federation of Sewage & Indust. Wastes Ass., Research Committee (Heukelekian, H., Chairman). **A Review of the Literature of 1958 on Sewage, Waste Treatment, and Water Pollution.** *Sewage & Indust. Wastes.* Wash. 1959, May, June & July, v. 31, Nos. 5, 6 & 7, 501–41; 615–61; 763–803. [Numerous refs.]

Food and Nutrition

FOODSTUFFS

Composition and Bacteriological Control

Trimarchi, G. Il controllo batteriologico delle stoviglie nei pubblici esercizi: 1) Metodi per la determinazione della carica batterica. [**The Bacteriological Control of Food Utensils in Public Service. (1) Methods for the Determination of the Bacterial Content**] *Igiene Moderna.* 1959, Jan.–Feb., v. 52, Nos. 1/2, 95–111. [14 refs.] English summary.

This is a preliminary report but the word " utensils " includes also crockery, glassware, etc. The author has been seeking a simple method of both quantitative and qualitative bacteriological control of the apparatus used by the public in restaurants, bars, etc.

He first made 6 comparative tests using raw cotton swabs dipped in (a) the buffered distilled water [Standard Methods, this *Bulletin*, 1944, v. 19, 723] and (b) the neutralizing buffer solution recommended in 1948 (*American Public Health Association, Standard Methods for an Examination of Dairy Products* [*ibid.*, 1950, v. 25, 209]). The swabs were streaked over the surface of plates, the internal and external rims of cups, and glasses, spoons, etc. There was no difference in the results. Next, the soluble calcium alginate (Calgitex) swab advocated by Higgins in 1950 [this *Bulletin*, 1950, v. 25, 725] was tested with the neutralizing buffer to see if it was satisfactory; this was the case.

Finally a comparison was made between the results after using the Calgitex swabs and the raw cotton swabs in the neutralizing buffer solution. After plates had been used and washed with the usual detergents, each type of swab was streaked over one-half of the surface of 5 plates. 15 tests were carried out, and the Calgitex swabs proved superior in each one.

The author considers therefore that (1) the Calgitex swabs are very useful for the bacteriological examination of eating utensils; (2) the neutralizing buffer solution is better than buffered distilled water; (3) trypto-glucose-beef-agar gave excellent results as a culture medium. *W. K. Dunscombe*

Ministry of Health. **The Ice-Cream (Heat Treatment, etc.) Regulations, 1959.** Circular 8/59. 5 pp. 1959. London: H.M. Stationery Office. [6d.]

The main clauses and new requirements are as follows—water ices and ice lollies, whether containing milk solids or not, that are mixed before freezing and have a *p*H value of 4·5 or less, have been exempted from the prescribed heat treatment provisions. A *p*H meter can be used. This is expensive and its operation requires some skill but a special indicator paper test can provide a ready means of checking the approximate *p*H level of acidity.

Regulation 5 (ii) now permits a sterilization process as an alternative to pasteurization. A mixture sterilized in the prescribed manner and canned immediately under sterile conditions need not be cooled to and kept at a temperature of 45°F. or below unless and until the can is opened.

As regards composite mixtures a new proviso allows the temperature of a heat-treated ice-cream mix to rise temporarily above 45°F. when added to a water ice or ice lolly mixture with a *p*H value of 4·5 or less, but the combined mixture must be frozen within one hour.

An Appendix gives detailed advice on the bacteriological examination of ice-cream. *W. G. Savage*

Névot, A., Lafont, P. & Lafont, J. De la destruction des bactéries par la chaleur. Étude de l'efficacité de la pasteurisation du lait. [**Destruction of Bacteria by Heat. Study of the Efficacy of Pasteurisation of Milk**] *Bull. Acad. Nat. Méd.* 1959, v. 143, Nos. 9/10, 175–82, 1 fig. & 3 graphs.

The paper deals with 2 series of experiments in the laboratory on the destruction of pathogenic organisms

which might be found in milk and on the efficacy of the pasteurization of milk.

The first part sets out in tabular form the times taken at a temperature of 72°C. to destroy pathogenic organisms which might possibly be found in milk. The vehicles used were raw milk and sterilized milk. Under these conditions bovine tubercle bacilli in culture were destroyed in a materially shorter time (4 to 9 minutes) than the human strains (8 to 12 minutes) and the same applied when pathological products were used.

A laboratory pasteurization plant on the lines of the HTST (High Temperature Short Time) type was used for another series of tests and the destruction times of human and bovine tubercle bacilli and other pathogens at 72°C. are shown. For the tuberculosis strains an exposure of 2 minutes was found effective. Some experiments on the destruction of phosphatase confirm its diagnostic value as a test for the efficiency of pasteurization. *W. G. Savage*

Miscellaneous Diseases

LIEBESCHUETZ, H. J. **Respiratory Signs and Symptoms in Young Soldiers and their Relationship to Smoking.** *J. Roy. Army Med. Corps.* 1959, Apr., v. 105, No. 2, 76–81.

147 men of a Parachute Brigade of very high physical standard were specially questioned at their release medical examination. Of 83 cigarette smokers 57 (69%) had no symptoms or signs of chest disease (cough, sputum, rhonchi). Of 52 non-smokers as many as 51 (98%) had no symptoms or signs (the one exception had rhonchi). The incidence of abnormal signs or symptoms showed an increase with number of cigarettes smoked. In short, quite a large proportion of these very fit young men had some degree of respiratory abnormality and, in such a group where other possible causes are largely excluded, the incidence was almost entirely confined to smokers. Their general health at that time was not affected but individual case histories show that more severe symptoms can be produced by smoking. *A. Bradford Hill*

SASLAW, M. S. & STREITFELD, M. M. **Correlation of Smoking Habits with Hemolytic Streptococci and Antistreptolysin O Responses.** *Amer. J. Med. Sci.* 1959, June, v. 237, No. 6, 754–8.

A survey of the distribution of β haemolytic streptococci in the throats of healthy adults provided an opportunity for examining the frequency of the occurrence of the organisms in relation to smoking habits. Data for 1,812 throat swabbings showed that β haemolytic streptococci were isolated about twice as frequently from present smokers as from non-smokers and past smokers (13·1% against 6·3% and 7·8%). All types of β haemolytic streptococci examined showed similar differences. Antistreptolysin O titre showed no appreciable differences between the sera of the 3 classes of persons. It is suggested that the observed differences might be due to an effect of smoke products on streptococci or on the mucous membrane barrier of the host.

[Data are given separately for the frequency of isolation of streptococci among men and women and among white and coloured persons in each smoking category. Unfortunately there is no similar breakdown for the total numbers of smokers and of non-smokers, and it is possible that differences in smoking habits between the various sex and social groups could have affected the result.] *Richard Doll*

Bacteriology and Immunity

Abstracts of papers relating to the bacteriology of plague, cholera, yaws, leprosy and certain other tropical bacterial diseases; of the rickettsial fevers; and of yellow fever, dengue, rabies and certain other tropical virus infections, are published in the TROPICAL DISEASES BULLETIN. *Their titles and page references are cited below in the appropriate sub-division of this section*

GENERAL

SNEATH, P. H. A. & COWAN, S. T. **An Electro-Taxonomic Survey of Bacteria.** *J. General Microbiol.* 1958, Dec., v. 19, No. 3, 551–65, 3 figs. [19 refs.]

By the techniques previously described [this *Bulletin*, 1957, v. 12, 1181], the relationship of 60 strains of bacteria from the National Collection in London were analysed by the electronic computer. These strains of bacteria covered 5 main groups: (1) Gram-positive organisms—all the cocci, some diphtheroids, *Erysipelothrix*, *Listeria*; (2) mainly Gram-negative organisms, enterobacteria, pseudomonads, *Pasteurella*, *Vibrio*, *Brucella* among others, and the *Bacillus* group; (3) *Corynebacterium diphtheriae*; (4) acid-fast bacilli; (5) spirilla.

The results showed that the 5 groups are distinct, but in the Gram-positive and negative bacteria there are sub-groups showing similarities. There is a close similarity as would be expected between the streptococci, the micrococci and diphtheroids. The unexpected finding is the closeness of the *Bacillus* and *Pasteurella septica*, *Brucella*, *Neisseria*, and *Actinobacillus* to the enterobacteria, and the dissimilarity of *Proteus* to the latter.

This is a preliminary survey indicating where further work can be done. A most important essential in taxonomic work is a defined bacterial type strain. Where this was lacking in the groups studied the authors chose what they consider to be suitable temporary working type strains which could be used as reference strains for future work and even perhaps as future type strains. [Their choices may well be controversial.] The value of old laboratory records and the errors found in human observations are discussed.

[This paper is a fascinating "must" for all who are either interested in or bored by the problems of bacterial classification and taxonomy.]

Elizabeth M. Harper

STOCKER, B. A. D. **Bacterial Genetics and Infectious Disease.** *Amer. J. Human Genetics.* 1959, June, v. 11, No. 2, Pt. 2, 354–65. [21 refs.]

This admirably clear account thoughtfully discusses some interesting work which will introduce even timid readers most helpfully to such conceptions as—for example: variation and dissociation; genetic recombination; spontaneous mutation and selection; transformation; transduction; mating; and the transfer of F factor and of colicinogenicity. Moreover, the author shows how such phenomena are related to problems familiar to medical bacteriologists either in their routine work or in their animal experiments designed to clarify the problems of infectious disease. Thus the study of the hereditable characters of bacteria is shown to be relevant to such problems as virulence, active immunization, bacterial strains resistant to antibiotics, the rival conceptions of minimum lethal dose or independent action, phage-typing, typhoid carriers, and the spread of bacteria within the tissues of the host.

Reasons are given for the view that, in the natural phenomena of infectious disease, spontaneous mutation and selection by themselves can account for the observed instances of changes of hereditary character among the causal micro-organisms. The methods used in studying bacterial heredity, however, have much to contribute as tools for the investigation both of infectious disease and the underlying problems of bacterial variation.

J. W. Howie

STUART, R. D. **Transport Medium for Specimens in Public Health Bacteriology.** *Pub. Health Rep.* Wash. 1959, May, v. 74, No. 5, 431–8. [20 refs.]

When Stuart first introduced his transport medium [this *Bulletin*, 1946, v. 21, 620] its value was at once recognized in venereal clinics for the culture of gonococci from the cervix where immediate laboratory facilities were not always available. It has, of course, wider uses and the author now writes of his further experiences of the medium in public health bacteriology in Canada.

The principles involved in designing the medium were the prevention of oxidation and the elimination of all nutrients so that the specimen could be preserved in the state in which it was collected until the appropriate time when it could be inoculated onto the medium of choice in the laboratory or examined directly by the bacteriologists. The medium is essentially a soft water-agar gel, soft enough not to crack and allow exposure of the specimen yet hard enough to prevent agitation during transport. It contains sodium thioglycolate and the *p*H is stabilized by a phosphate buffer (calcium glycerophosphate); methylene blue is added. Specimens are collected on a wool-swab on a wood-stick. The swab is boiled in buffer and then impregnated in charcoal before issue; immediately after collection the swab is thrust into the transport medium in its container, the upper part of the stick broken off and the container sealed until the bacteriologist is ready to deal with it.

Although many workers are critical of the use of rectal swabs for the investigation of outbreaks of dysentery there are occasions when this is the only practical means of collecting specimens from large numbers of individuals. Dr. Stuart speaks well of the medium for this purpose.

H. J. Bensted

AMSTERDAM, D. & SCHNEIERSON, S. S. **Mucin-Like Enhancement of Microbial Virulence for Mice by Bile Salts and Certain Surfactants.** *Proc. Soc. Exper. Biol. & Med.* 1959, June, v. 101, No. 2, 396–8.

Preliminary experiments with a mixture of sodium taurocholate and sodium glycocholate injected into mice indicated that bile salts could greatly increase the mouse-virulence of *Staphylococcus aureus* [this *Bulletin*, 1958, v. 33, 1070]. Following these results the possibility of other surface agents having a pathogenizing activity was examined. Di-isopropyl naphthalene sodium sulphonate (Naccosal A), di-hexyl sodium sulphosuccinate (Aerosol MA), alkyl-aryl-polyether alcohol (Triton X-100), polyoxyethylene sorbitan monooleate (Tween-80), bile salts and mucin in suitable concentrations, mixed with a standard dose of *Salmonella typhi*, were injected intraperitoneally into mice (10 mice were used for each test; the 10 control mice received the same dose of *Salm. typhi* in normal saline). In the control mice and those receiving Tween + organisms only one mouse in each group died, but the figures for the other substances were: mucin 9/10, bile salts 8/10, Naccosal, Aerosol A and Triton 10/10. Mucin had a viscosity one and a half times that of the other agents so that viscosity and pathogenizing activity would not appear to be correlated. This mucin-like effect of bile salts, Naccosal, Aerosol A and Triton on the mouse-virulence of *Salm. typhi* is quoted here as an example; several other organisms were examined and results of the same order were obtained with these reagents. Tween-80 regularly failed to exhibit the same properties. The authors suggest that a substance such as Triton X-100 could be used as a satisfactory replacement for mucin in tests for mouse-virulence of organisms since it has a defined chemical constitution.

H. J. Bensted

CHAPMAN, G. B. **Electron Microscopy of Ultrathin Sections of Bacteria. III. Cell Wall, Cytoplasmic Membrane, and Nuclear Material.** *J. Bacteriology.* 1959, July, v. 78, No. 1, 96–104, 14 figs. [29 refs.]

RICHOU, R. Les diastases des micro-organismes leurs propriétés—leur rôle. Leur utilisation dans la pratique. [**The Diastases of Micro-organisms; their Role and Utilization in Practice**] *Rev. d'Immunologie.* 1959, Apr.–June, v. 23, No. 3, 196–223. [Refs. in footnotes.]

BENACERRAF, B., THORBECKE, G. J. & JACOBY, D. **Effect of Zymosan on Endotoxin Toxicity in Mice.** *Proc. Soc. Exper. Biol. & Med.* 1959, Apr., v. 100, No. 4, 796–9. [14 refs.]

Tolerance of animals to endotoxin resulting from pretreatment with endotoxin is accompanied by increased phagocytic activity of the reticulo-endothelial system [BIOZZI, BENACERRAF and HALPERN, this *Bulletin*, 1955, v. 30, 1127]. The present work showed that repeated injections of zymosan into mice were also associated with increased phagocytic activity, but in contrast the animals were 50–100 times more susceptible to endotoxin than normal controls. The increased susceptibility of zymosan-treated mice to endotoxin was almost completely abolished when the challenge was preceded by cortisone or hydrocortisone. The normal mice cortisone gave very little protection against endotoxin. In BCG-infected mice there is also increased activity of the reticulo-endothelial system and increased susceptibility to endotoxin [SUTER *et al., ibid.*, 1959, v. 34, 279; HALPERN *et al., loc. cit.*] Experiments are described which confirm this and it was found that, as in the zymosan-treated animals, cortisone greatly reduced the lethal effect of endotoxin.

It is suggested that the increased susceptibility to endotoxin may be explained by increased susceptibility of the reticulo-endothelial system or by interference with the level of adrenal hormones. The latter view is favoured by the authors. *Douglas D. Smith*

LEQUIRE, V. S., HUTCHERSON, J. D., HAMILTON, R. L. & GRAY, M. E. **The Effects of Bacterial Endotoxin on Lipide Metabolism. I. The Responses of the Serum Lipides of Rabbits to Single and Repeated Injections of Shear's Polysaccharide.** *J. Exper. Med.* 1959, Aug. 1, v. 110, No. 2, 293–309, 3 figs. [30 refs.]

RAYNAUD, M., RELYVELD, E. H., TURPIN, A. & MANGALO, R. Préparation d'anatoxines diphtérique, tétanique et staphylococcique de haute pureté, adsorbées sur phosphate de calcium (brushite). [**Preparation of Highly Purified Diphtheria, Tetanus and Staphylococcal Toxoids adsorbed on Calcium Phosphate**] *Ann. Inst. Pasteur.* 1959, Jan., v. 96, No. 1, 60–71, 1 fig. [29 refs.]

The authors emphasize the advantages of preparing toxins of high purity before proceeding to the conversion of these to toxoid since complete detoxification can be obtained with smaller amounts of formaldehyde, the toxin being reduced to amounts unrecognizable in animal tests in 2–5 days. The advantage of producing a precipitate of Ca phosphate in actual contact with the solution of toxoid is also stressed and details of the optimal concentrations and reaction for this procedure are given. The quantities of formaldehyde required relatively to the Lf concentration of toxin or, in case of staphylococcal toxin, the LH concentration, are given for each toxin, and also tables to show the rates at which the detoxification proceeds with each.

J. W. McLeod

BACTERIOSTATIC AND BACTERICIDAL SUBSTANCES; DISINFECTION

In this section the abstracts are arranged as far as possible in the following order: General; Antibiotics; Other Therapeutic Substances; Disinfection.

ANN. INST. PASTEUR. 1959, July, v. 97, No. 1, 1–103. [Numerous refs.] Colloque annuel de la SOCIÉTÉ FRANCAISE DE MICROBIOLOGIE. Evolution des bactéries et de l'aspect des infections sous l'influence des antibiotiques. **[Annual Colloquium of the French Society of Microbiology. Changes in Bacteria and in the Characters of Infections under the Influence of Antibiotics].**

This report comprises 9 contributions on a few aspects of the subject chosen, with particular emphasis on only one: 5 papers and almost exactly half the printed space are devoted to tuberculosis. The contributions include a general introduction by C. GERNEZ-RIEUX (pp. 1–6) and a final brief appraisal by J. REILLY (pp. 101–3): the remainder consists of 5 papers, and 2 items under the heading "Discussion".

R. FASQUELLE (pp. 7–40) deals with changes in the characters of infections. The evolution and prognosis of antibiotic-susceptible infections have been profoundly altered: instances cited are the effect of penicillin on acute haemolytic streptococcus infection, whether at the stage of lymphangitis or of septicaemia. The prognosis in bacterial endocarditis has been immensely improved, but a patient in whom the infection has been eliminated may still die of heart failure. Similarly *Clostridium welchii* septicaemia following abortion is easily preventable and in early stages curable, but if treatment is delayed death may still occur from uraemia. This is a late effect from the action of exotoxins: the liberation of endotoxins, as in typhoid fever, may also have a serious effect. Other subjects discussed are the effects of antibiotic treatment on serological tests and on the development of immunity, and changes in mortality and morbidity generally.

Y. CHABBERT (pp. 41–52) deals with effects on the micro-organism, under the title *Evolution of Resistant Bacterial Populations under the Influence of Antibiotics*. This much briefer contribution discusses first how resistance develops within a single species, and secondly how under the influence of antibiotic treatment resistant species attain predominance in mixed populations. The "germs of the future" emerging in this way are staphylococci and coliform bacilli (*Pseudomonas* spp. etc.).

G. CANETTI (pp. 53–79) in a long contribution entitled *Changes in the Populations of Tuberculous Foci during Chemotherapy*, distinguishes 3 kinds of effect on tubercle bacilli. They may be killed, and extensive results are quoted showing that cavities are often sterilized. In such areas as caseous foci, where conditions are unfavourable for their growth, the bacilli are consequently less susceptible to the action of the drug, and then simply "persist". Thirdly, they may acquire resistance: conditions favouring this change are discussed, and measures for preventing it, with emphasis on adequate dosage and the use of drug combinations.

N. RIST (pp. 80–87) writes on *The Pathogenicity of Isoniazid-Resistant Tubercle Bacilli*. There are intermediate stages between the normal organism and the highly isoniazid-resistant catalase-negative bacillus incapable of causing progressive disease in the guineapig. One reason for not regarding this change with complacency or approval is that at intermediate stages virulence may be unaltered, and bacilli at all stages may exist in the same patient: Secondly, lack of virulence for the guineapig must not be assumed to involve diminished virulence for man: even meningitis has been caused in patients by such organisms. Therefore treatment should be so directed as to discourage the appearance of isoniazid resistance, and patients infected with resistant bacilli should be isolated just as strictly as others.

B. KREIS (pp. 88–94) discusses *Enzymatic Changes in Isoniazid-Resistant Bacilli*. Resistant strains are often catalase-positive, and among those that are, the degree of catalase activity is not proportional to the degree of resistance. On the other hand, there is a very close correlation between resistance and loss of peroxidase activity: of 146 sensitive strains 143 were peroxidase-positive; of 137 resistant strains only 12 were found positive, and in 9 of these tests an error was found to have been made. Loss of peroxidase activity offers no explanation for loss of virulence, but loss of catalase activity does, because it renders the bacilli susceptible to H_2O_2 formed in the tissues. Tests of capacity to form these enzymes offer a rapid means of identifying isoniazid-resistant bacilli.

The succeeding brief contribution to "Discussion" by the same author simply concerns the clinical interpretation of tests of bacillary resistance, emphasizing that these can be directly translated into therapeutic terms.

A. TACQUET (pp. 98–100) finally reports some original observations showing that avian tubercle bacilli rendered highly isoniazid-resistant *in vitro* became completely avirulent for both chickens and rabbits.

Most of these papers contain little or nothing that has not already been published elsewhere, but those of Canetti, Rist and Kreis are useful reviews on particular aspects of tuberculous infection. The only 2 papers dealing with the general subject are perhaps necessarily less helpful because to deal adequately with so wide a field necessitates a good deal of stating the obvious. *L. P. Garrod*

MURAT, Anne M., STINEBRING, W. R., SCHAFFNER, C. P. & LECHEVALIER, H. **Screening for Antibiotics active against Intracellular Bacteria.** *Applied Microbiol.* Baltimore. 1959, Mar., v. 7, No. 2, 109–12.

This screening method, in which crude culture filtrates of new antibiotic-producing actinomycetes are used, is designed to afford much more information than is usually obtained at this stage: it affords a test of both toxicity to and capacity to penetrate mammalian cells. *Brucella abortus* suspension is added to living monocytes obtained after injecting saline into a guineapig's peritoneal cavity: phagocytosis follows, and the cell + bacterial suspension is placed in tubes where the cells adhere to the glass. To these are added a mixture of

guineapig serum and actinomycete culture filtrate, with a small amount of streptomycin to kill remaining free bacteria. If many of the monocytes appear dead after 1 day's incubation the tube is discarded: if not, incubation is continued for a further day, and the fluid is then removed and replaced with nutrient agar. Surviving organisms produce colonies in this, and a reduction in the number of these colonies is taken to indicate intracellular antibiotic action. In tests with pure antibiotics, oxytetracycline and chloramphenicol exerted such action in low concentrations, streptomycin, neomycin and polymyxin only in high. When the method was applied to recently isolated actinomycetes, the 52nd product had the desired activity: subsequent investigation showed that the antibiotic formed by the freshly isolated actinomycete was chloramphenicol. [The authors do not mention the work of G. B. MACKANESS (this *Bulletin*, 1953, v. 28, 612), who pioneered the study of the intracellular action of antibiotics, and used a method similar to this.] *L. P. Garrod*

NAUMANN, P. Zum Problem der bakteriologischen Resistenzbestimmung bei lokaler Antibiotica-Therapie. Methode zur Konzentrationsbestimmung am Wirkungsort. [**On the Problem of determining bacterial Resistance in connection with local Antibiotic Treatment. Method for determining Concentration at the site of Infection**] *Ztschr. f. Hyg. u. Infektionskr.* 1958, v. 145, No. 4, 395–402, 2 figs. [15 refs.]

Tests of bacterial sensitivity to antibiotics given systemically are based on concentrations attainable in the blood. Those attained by local application are not so well known. To determine these, at least for one preparation and one site of application, 100 mgm. of Nebacetin cream (Nebacetin contains neomycin and bacitracin) was placed in the lower conjunctival sac of 30 normal subjects, and at intervals of 5 to 160 minutes a 6 mm. filter paper disk was introduced and left *in situ* for 2 minutes to absorb secretion. These disks were dried and placed on the surface of medium pre-seeded by flooding with *Staphylococcus aureus*. By comparison of the inhibition zones produced, with those produced by disks containing known amounts of Nebacetin, the content of the unknowns could be determined (a large and beautifully prepared plate showing such a test is illustrated). The averaged results in all subjects are presented as a graph showing a steep fall in content during the first 20 minutes, succeeded by a slower fall, diminishing amounts of the antibiotic still being present up to 2½ hours.

L. P. Garrod

LAWRENCE, J. C. **The Comparative Toxicity of Antibiotics to Skin.** *Brit. J. Pharmacol. & Chemotherapy.* 1959, June, v. 14, No. 2, 167–73, 2 figs. [19 refs.]

These experiments were performed, with closely concordant results, with both guineapig and human skin, respectively cut from the dorsum of the ear and left over from the grafting of burns. They were of 2 kinds, measurements of respiration continued at intervals for 24 hours, and observations of growth in tissue cultures for 3 days: the medium used for both purposes contained 50 μgm./ml. of streptomycin. Concentrations of antibiotics which depressed respiration by 30% also inhibited growth in tissue culture: those depressing it by 60% usually produced necrotic cultures. 16 antibiotics in all were tested: the more important of these may be classified according to results as follows. Erythromycin, oleandomycin and bacitracin have negligible toxicity in saturated solution; chloramphenicol, streptomycin, neomycin and vancomycin have a toxicity of the same order as that of penicillin: the tetracyclines, novobiocin and polymyxin are many times (35–108) more toxic than penicillin.

These studies were made at the Medical Research Council Industrial Injuries and Burns Research Unit, Birmingham, with a view to determining whether local antibiotic treatment of burns can do any cellular damage. [The results seem reassuring. Toxic concentrations are stated in mgm./ml., and the lowest found was 0·2—*i.e.* 1 part in 5,000.] *L. P. Garrod*

BOYCE, S. F. & VAIDYA, S. S. **Penicillin Salts of Steroidal Amines. I. Chemistry.** *Antibiotics & Chemotherapy.* New York. 1959, June, v. 9, No. 6, 358–63, 2 figs. [12 refs.] **II. A Comparative Study of Physical and Chemical Properties.** *Ibid.*, 364–8, 2 figs.

i. "Preparation of penicillin salts of N-benzyl-3β-cholesterylamine, N-benzyl-6β-amino-3 : 5-cyclocholestane and N-(cyclohexylmethyl) cholestan-3β-ylamine have been described. Correlation of penicillin blood serum levels with chemical constitution is discussed briefly."

ii. "Some physical and chemical properties of N-benzyl-3β-cholesterylamine penicillin G, N-benzyl-6β-amino-3 : 5-cyclocholestane penicillin G, and N-(cyclohexylmethyl) cholestan-3β-ylamine penicillin G have been described. These properties include determination of solubility in different organic solvents, solubility in water (by bioassay), melting point, elemental composition, specific optical rotation, ultraviolet absorption, infrared spectra, potency, and stability of the salts at acid *p*H."

HUMPHREY, J. H., LIGHTBOWN, J. W. & MUSSETT, Marjorie V. **International Standard for Phenoxymethylpenicillin.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 6, 1221–7, 1 fig.

SEDLACZEK, L., CZERNIAWSKI, E. & ZABŁOCKI, B. **The Specific Protective Effect of Lipo-Polysaccharide-Protein Symplexes Isolated from *Escherichia coli* on the Sensitivity of Gram-Positive Bacteria to Penicillin.** *Bull. Acad. Polonaise des Sci.* Warsaw. Sér. Sci. Biol. 1959, v. 7, No. 5, 173–6.

These authors have previously shown that "lipo-polysaccharide-protein symplexes" isolated from Gram-negative bacilli protect staphylococci against penicillin. In an example presented here, such a substance from

Escherichia coli when added to a suspension of *Staphylococcus aureus*, raised the minimum inhibitory concentration of penicillin for this organism from 0·06 to 64 μgm./ml. The authors believe that the substance is adsorbed on the surface of the Gram-positive cell and prevents its penetration by the antibiotic. These observations are here extended in 2 ways: (1) by showing that the substance does not protect staphylococci against streptomycin, chloramphenicol, chlortetracycline or oxytetracycline; (2) by tests of its capacity to protect other Gram-positive organisms against penicillin. The increase in minimum inhibitory concentration produced by it for *Staph. aureus* being 1,028-fold, the corresponding factors for 5 other organisms were found to be *Staph. albus* 16, *Streptococcus pyogenes* 16, *Corynebacterium diphtheriae* 256, *Sarcina lutea* 8 and *Str. pneumoniae* 8. *L. P. Garrod*

ROSE, A. H. & MARTIN, S. M. **Studies on a Toxin-Inactivating Substance excreted by** *Penicillium cyaneo-fulvum*. *J. General Microbiol.* 1959, June, v. 20, No. 3, 451–61, 5 figs. [28 refs.]

This paper from the Division of Applied Biology, National Research Council, Ottawa, describes a continuation of the work of E. G. D. MURRAY and his colleagues [this *Bulletin*, 1959, v. 34, 557] on a toxin-inactivating substance produced by a strain of *Penicillium cyaneo-fulvum*. An improved method of assay was devised, in which the substance is added to an excess of staphylococcal α-toxin, and the diminution in haemolytic activity is then measured. Conditions for its production were studied: meat extract was found to be an essential constituent in the medium. The curve for its production as incubation proceeded closely followed that of developing protease activity: moreover, when the product was either concentrated by copper sulphate precipitation and ammonium sulphate fractionation, or destroyed by heat or di*iso*propylfluorophosphate, toxin-inactivating and protease activity ran closely parallel. It therefore seems probable that the toxin-inactivating substance is a proteolytic enzyme. In view of the fact that in the original study staphylococcal α-toxin was shown to be inactivated without loss of antigenicity ("toxoiding" effect) it is interesting that pepsin has previously been shown to have the same effect on this toxin. *L. P. Garrod*

SEIGNEURIN, R., MAGNIN, R. & FILS, J. Résistance à l'hémolyse des hématies par adjonction d'antibiotiques (pénicilline-streptomycine). [**Erythrocyte Resistance to Haemolysis after Addition of Antibiotics (Penicillin-Streptomycin)**] *Ann. Inst. Pasteur*. 1959, May, v. 96, No. 5, 530–36, 6 figs.

Blood was collected in glucose-citrate solution containing antibiotics (200 ml. blood + 50 ml. solution containing 500,000 units of "bipenicillin" and 0·5 gm. dihydrostreptomycin) and stored at 4°C. Fragility tests (*i.e.*, addition of blood to saline of different degrees of hypotonicity, which was then centrifuged, the free haemoglobin being estimated colorimetrically) were conducted at intervals. Graphs [apparently drawn freehand, with no points on them] show the findings after 1, 7, 12, 19, 33 and 47 days of storage, comparison being made with the same blood taken into glucose-citrate without antibiotics. All show the antibiotic-containing blood to be somewhat more resistant to lysis. It is suggested that in patients requiring both transfusion and treatment with these antibiotics, their addition to blood might be useful, both in increasing red cell resistance, and because cells on which antibiotics are adsorbed acquire "itinerant bactericidal properties". When oxytetracycline (125 mgm. to 200 ml. blood) was added instead, resistance to lysis was diminished [no details given]. *L. P. Garrod*

HUMPHREY, J. H., LIGHTBOWN, J. W. & MUSSETT, Marjorie V. **The Second International Standard for Streptomycin.** *Bull. World Health Organization*. Geneva. 1959, v. 20, No. 6, 1233–9, 1 fig.

LODER, R. E. & WALKER, G. F. **Neuromuscular-Blocking Action of Streptomycin.** *Lancet*. 1959, Apr. 18, 812–13.

Neomycin in normal and streptomycin in large doses have been shown experimentally to produce neuromuscular block. These authors from Peterborough give the histories of 3 patients in whom treatment with 1 gm. streptomycin daily for 1 and 3 months and 3 days respectively apparently caused muscular weakness, accompanied in two of them by blurred vision: normal vision was immediately restored by giving neostigmine and this treatment also relieved or prevented recurrence of the general weakness. *L. P. Garrod*

KINOSHITA, T. **Studies on the Mode of Action of Streptomycin (SM), especially in connection with the binding of SM by** *M. avium*. *Nagoya J. Med. Sci.* 1958, Dec., v. 21, No. 4, 323–32, 10 figs. [15 refs.]

PRESCOTT, B., KAUFFMANN, Gladys & JAMES, W. D. **Means of increasing the Tolerated Dose of Streptomycin in Mice.** *Antibiotics & Chemotherapy*. New York. 1958, Jan., v. 8, No. 1, 27–32.

"Streptomycin was found to be 50 per cent lethal in a dose of 7.5 mg. (375 mg./Kg.) and 92 per cent lethal in a dose of 10 mg. (500 mg./Kg.) by subcutaneous administration in white mice. By the use of various adjuvants, it has been found possible to protect mice against two or even three times the lethal dose. Glycine and/or sodium glucuronate permitted tolerance of 20 mg. streptomycin, with optimal results obtained when both were used. Sodium salts of two alpha-keto acids, alpha-ketoglutaric and pyruvic acid, increased the tolerated dose to 20 and 30 mg. with 85 per cent and 64 per cent survival, respectively. Aqueous glycerine (35 per cent) or aqueous propylene glycol (75 per cent) solutions enabled most of the animals to survive 15 and 20 mg. of streptomycin, respectively. Of the series, only glycerine has been tested for its effect on chronic toxicity, with the result that 19 of 21 mice survived 14 semiweekly administrations of 10 mg. streptomycin in 35 per cent glycerine

solution. In a control test of the adjuvants, only glycerine in concentrations of more than 15 per cent inhibited the in vitro growth of an avirulent strain of *Mycobacterium tuberculosis*. Streptomycin inhibition was not affected by any of them except by glycerine, which enhanced the streptomycin tuberculostatic activity."

PRESCOTT, B., KAUFFMANN, Gladys, JAMES, W. D. & STONE, H. J. **Means of increasing the Tolerated Dose of Streptomycin in Mice. II. Certain Vitamins.** *Antibiotics & Chemotherapy.* New York. 1959, June, v. 9, No. 6, 369–75. [21 refs.]

A single subcutaneous dose of 10 mgm. of streptomycin caused 93% mortality in a strain of albino mice (88% in the DBA. strain). When the dose was previously mixed with calcium pantothenate (1·75–14 mgm.) nicotinic acid (1–36 mgm.), ascorbic acid (2·5–30 mgm.), *p*-aminobenzoic acid (10–20 mgm.), inositol (13–26 mgm.) or isonicotinic acid (15–36 mgm.) the mortality was greatly reduced, in a few instances to nil, and usually more by the larger doses of these substances. With the exception of inositol, they were also shown to reduce the mortality from daily repetition of this dose of streptomycin for 20 days, calcium pantothenate being the most effective and nicotinic acid next (90 and 80% survival respectively). None of these substances interfered with the inhibitory action of streptomycin on the growth of *Mycobacterium tuberculosis in vitro*. Riboflavin, folic acid, thiamine hydrochloride, choline hydrochloride, pyridoxine hydrochloride, pyridoxal hydrochloride, nicotinamide, biotin and menadione were tested in the same way and found to have little or no effect in protecting against the toxic effect of streptomycin. *L. P. Garrod*

LARKIN, R., with the microbiological assistance of W. W. HESELTINE. **Side-Effects of Tetracycline alone and of Tetracycline with Nystatin.** *Lancet.* 1959, June 13, 1228–9.

There is conflicting evidence about the capacity of nystatin to prevent gastro-intestinal side-effects in patients given tetracycline. Tetracycline was given in a dose of 250 mgm. 4 times a day to 98 adults "mainly with acute or chronic respiratory infections": 55 received it alone and 43 together with 250,000 units of nystatin 4 times a day. Gastro-intestinal disturbances, chiefly consisting of distension and general discomfort or nausea, occurred in 67% of the group given tetracycline alone and in only 9% of those given nystatin: corresponding percentages for diarrhoea were 16 and 0, and for pruritus ani 24 and 5. [The duration of treatment is not mentioned, nor the time of onset of these symptoms.] In the later patients, rectal and throat swabs were taken on the 5th day and examined for *Candida albicans* and other yeasts: they were more often found in both situations in the tetracycline alone group, 3 of whom actually developed oral thrush.
L. P. Garrod

CARLSON, J. R. & SYNDER, Jean W. *Candida albicans* **Plate Assay of Nystatin.** *Antibiotics & Chemotherapy.* New York. 1959, Mar., v. 9, No. 3, 139–44, 1 fig.

HUMPHREY, J. H., LIGHTBOWN, J. W. & MUSSETT, Marjorie V. **The International Standard for Polymyxin B.** *Bull. World Health Organization.* Geneva. 1959, v. 20, No. 6, 1229–32.

JENEY, E. & ZSOLNAI, T. Versuche zur chemotherapeutischen Beeinflussung der durch gramnegative Krankheitserreger hervorgerufenen Infektionen der Harnwege und der Wunden. [**On the Chemotherapy of Urinary and Wound Infections by Gram-negative Bacteria**] *Zent. f. Bakt. I. Abt. Orig.* 1959, v. 175, Nos. 1/2, 124–32.

These authors, dissatisfied with present available treatments for urinary tract and wound infections by Gram-negative bacteria, have examined 160 compounds for capacity to inhibit the growth of 5 species. These compounds, which are fully listed, with the quantitative results obtained, in a table occupying 4 pages, included phenol derivatives, chelating compounds, nitro- and nitroso-compounds, quinones, salts and compounds of heavy metals, organic sulphur compounds, several other classes of or individual synthetic substances, and antibiotics, of which 5 were tested. Of the organisms used *Staphylococcus aureus* was the most susceptible and *Pseudomonas pyocyanea* and *fluorescens* the least, with *Escherichia coli* and *Proteus vulgaris* intermediate in susceptibility. The authors seem somewhat discouraged by these findings, and in particular because even highly toxic substances have so little action on *Pseudomonas* spp.: only polymyxin seems to be of any avail against these organisms. [The findings for antibiotics indicate abnormal resistance: the strain of *E. coli* was totally resistant to polymyxin, which is most unusual, as were both *Pseudomonas* to streptomycin.] *L. P. Garrod*

DUTTON, A. A. C. & ELMES, P. C. **Vancomycin: Report on Treatment of Patients with Severe Staphylococcal Infections.** *Brit. Med. J.* 1959, May 2, 1144–9.

This paper describes in full the treatment with vancomycin of 9 patients with severe infections by staphylococci resistant to the more commonly used antibiotics. 5 had pneumonia or other infections of the respiratory tract, 2 wound infections, 1 peritonitis and 1 septicaemia: blood cultures were also positive in 1 case each of wound infection and pneumonia. 5 patients recovered: 2 died of the original infection and 2 of complicating *Pseudomonas pyocyanea* septicaemia. The usual total daily dose was 1 or 2 gm. intravenously. In 4 patients the treatment resulted in severe deafness and in 2 others this effect was suspected but the mental condition before death prevented its confirmation. 5 of these 6 patients had very high blood urea levels before treatment was begun and in the other the blood urea rose during treatment. The patients in whom deafness was not produced had a low or normal blood urea. It was therefore evident

that impaired renal function must lead to the accumulation of the antibiotic in the blood, unless the dose is accordingly reduced. A rapid assay method was therefore devised (a tube dilution method, the tubes being shaken during incubation and read after 5 hours) which could be performed daily and thus determine the dose to be given. Details of an anuric patient with staphylococcal pneumonia in whom treatment was so controlled are given: the initial assay after a dose of 500 mgm. showed 33 μgm./ml. and no antibiotic was given the next day; thereafter for 6 days only 250 or 375 mgm. were required to keep the blood level at about 5–12 μgm./ml. Only a total of 5·125 gm. was given in 11 days: the treatment was successful and hearing was unimpaired. "Serum vancomycin assays are now undertaken routinely with patients having a raised blood urea." [Since 2, 3 or even 4 assays were made daily in the case described, not many hospital laboratories will find it possible to emulate this precaution.] *L. P. Garrod*

Berger, U. Die Wirkung des Vancomycin gegenüber oralen Spirochäten und Fusobakterien. [**The Action of Vancomycin on Oral Spirochaetes and Fusobacteria**] *Arch. f. Hyg. u. Bakt.* 1959, June, v. 143, No. 4, 316–20. [16 refs.]

This is another paper in a series by this author on the *in vitro* activity of more recently discovered antibiotics against non-sporogenous anaerobes. Under the conditions of test vancomycin inhibited 1 strain of *Borrelia vincenti* in a concentration of 0·5 μgm./ml., 6 strains of *Treponema microdentium* at 10, 12·5 or 15 μgm./ml., whereas 10 strains of *Fusobacterium* were not inhibited by 100 μgm./ml. [Lack of identification as to species detracts from the interest of the last-named finding.] Subsidiary experiments were done to show that 0·1% thioglycollate or agar in the medium used does not interfere with the action of the antibiotic. *L. P. Garrod*

Cronk, G. A. & Naumann, D. E. **The Absorption and Excretion of Kanamycin in Human Beings.** *J. Lab. & Clin. Med.* 1959, June, v. 53, No. 6, 888–95, 5 figs.

These workers in the Department of Health and Preventive Medicine of Syracuse University, New York, administered kanamycin intramuscularly to healthy volunteers and determined the amounts in the blood and urine at intervals after single and repeated doses. The maximum concentration in the blood was found 1 hour after the dose, and after doses of 1, 0·5 and 0·25 gm. averaged about 37, 23 and 14 μgm./ml. respectively: these levels fell to about 8–2 μgm./ml. after 8 hours [the diagrams conveying this information cannot be read with exactitude]. By giving repeated doses at different intervals, no course exceeding 3 days, information was obtained about the dosage required to keep the blood concentration above certain minima: these tests also show that there is no cumulative effect. 90% of the dose was excreted in the urine. Such findings were unaltered by bed rest or "ambulation", and by restricting or forcing fluids. No reaction occurred except pain at the site of injection in some subjects. Hyaline casts were found in some urines but no protein. *L. P. Garrod*

Griffith, L. J. & Ostrander, W. E. **A Comparison of the *In Vitro* Effectiveness of Kanamycin and Nine other Antibiotics against Staphylococci.** *Antibiotics & Chemotherapy.* New York. 1959, July, v. 9, No. 7, 416–18.

"Kanamycin appears from in vitro tests to be a highly effective drug against staphylococci. Sensitivity determinations indicated that relatively few of the clinical strains are resistant to kanamycin. Since many of the strains tested were resistant to penicillin, tetracycline, chloramphenicol, erythromycin and dihydrostreptomycin, it can also be concluded that organisms resistant to these commonly used antibiotics do not exhibit cross resistance with kanamycin."

Lustberg, A. & Hamburger, M. **Eighth Nerve Deafness after Administration of Kanamycin.** *J. Amer. Med. Ass.* 1959, June 13, v. 170, No. 7, 806.

Kanamycin can damage the eighth nerve: previous reports of this are briefly reviewed. A 52-year-old male diabetic in whom vascular complications had already resulted in coronary heart disease, blindness and gangrene necessitating amputation above both knees, developed boils on the head and arm which failed to respond to sulphisoxazole, chloramphenicol, tetracycline, erythromycin or penicillin. He was therefore given kanamycin 2 gm. intramuscularly daily in divided doses: the blood urea was then 27 mgm.%. Deafness was noted after 4 days, and thereafter urinary output was scanty and the blood urea rose to 64 mgm.%. Treatment was stopped after 13 gm. had been given. Deafness was almost complete and has remained so: there is also constant vertigo due to loss of vestibular function. [Whether this disastrous treatment also had any beneficial affect is not mentioned, nor is anything said about the sensitivity of the staphylococcus to the 6 drugs used.] *L. P. Garrod*

Antibiotics & Chemotherapy. New York. 1959, July, v. 9, No. 7, 419–38. **Psicofuranine. I. Discovery, Isolation, and Properties** [Eble, T. E., Hoeksema, H., Boyack, G. A. & Savage, G. M.], 419–20, 2 figs. **II. Studies in Experimental Animal Infections** [Lewis, C., Reames, H. R. & Rhuland, L. E.], 421–6, 1 fig. [13 refs.] **III. Production and Biological Studies** [Vavra, J. J., Dietz, A., Churchill B. W., Siminoff, P. & Koepsell, H. J.], 427–31. [11 refs.] **IV. Microbiological Assay** [Hanka, L. J., Burch, M. R. & Sokolski, W. T.], 432–5, 2 figs. [10 refs.] **V. Paper Chromatography and Ultraviolet Absorption Assay** [Sokolski, W. T., Eilers, N. J. & Eble, T. E.], 436–8, 2 figs. [13 refs.]

i. "The isolation and properties of psicofuranine, a new crystalline antibiotic from *Streptomyces hygroscopicus* var. *decoyicus*, are described."

ii. "The results of laboratory studies of a new antibiotic, psicofuranine, have been presented. The anti-

biotic was not active in vitro at practical levels, but in mouse-protection studies psicofuranine administered either orally or subcutaneously was effective against *M. aureus*, *S. hemolyticus* and *E. coli*. At the levels tested, it was inactive in *D. pneumoniae*, *P. vulgaris*, *Ps. aeruginosa*, and *Salmonella* infections. It was also inactive in experimental virus and nematode infections at the levels used.

"The antibiotic was capable of reducing the bacterial count of kidneys from mice having chronic *M. aureus* infections.

"It was not possible to induce resistance to psicofuranine in *M. aureus* by repeated exposures to the antibiotic in vivo. However, in vitro bacterial resistance to psicofuranine developed in a slow stepwise manner.

"A novel resistance-development pattern is reported in which *M. aureus* has been shown to develop resistance to an antibiotic that appears to have no in vitro inhibitory effect on that organism."

iii. "I. Psicofuranine is a new antibiotic produced by a streptomycete isolated from the soil. The organism is a variant of *Streptomyces hygroscopicus* and is designated as *Streptomyces hygroscopicus* var. *decoyicus*.

"2. A medium is described that will allow for production of psicofuranine in yields greater than 900 μg./ml.

"3. Psicofuranine shows in vitro activity against *E. coli*, *Sal. pullorum*, *Staph. aureus*, *Staph. albus*, and *Str. hemolyticus* in both agar dilution and broth dilution assays when special techniques are employed."

iv. "Psicofuranine, an antibiotic with antibacterial activity in vivo and without activity in vitro by the usual methods, was shown to have in vitro activity under special conditions. These conditions were: (1) the use of a semi-synthetic medium supplemented with liver extract; and (2) refrigeration of assay plates for four hours before incubation.

"The in vitro activity was used as a basis for three microbiological assay methods. The plate assay can detect a concentration of 10 μg./ml. psicofuranine in water and 3 μg./ml. in blood or blood serum. The turbidimetric assay can detect a concentration of 0·5 μg./ml. of psicofuranine in the growth medium. The test organism in all methods was *Staph. aureus* FDA-209P."

v. "The paper chromatographic pattern for psicofuranine with six solvent systems is described. Location of the antibiotic on paper strips is made by an ultraviolet light scanner.

"A physical method for the assay of psicofuranine in the presence of adenine and another compound with a similar ultraviolet absorption spectrum is described. The three compounds are separated by paper chromatography, and the developed paper strip is passed through a paper strip scanner attachment on an ultraviolet spectrophotometer. The optical density of the area on the strip that contains the psicofuranine is measured. The amount of psicofuranine on the test strips is determined from a standard curve plotted as logarithm dose versus optical density."

ORLANDELLA, V. & FERLAZZO, A. Ricerche *in vitro* sull'azione antibatterica della colimicina. [**Research on the *in vitro* antibacterial activity of Colimycin**] *Giorn. di Batteriol., Virol. ed Immunol.* 1959, Mar.–Apr., v. 52, Nos. 3/4, 134–41. [41 refs.] English summary (2 lines).

Colimycin, an antibiotic of polypeptide character produced by *Aerobacillus colistinus*, acts best on Gram-negative micro-organisms. The international unit is the smallest amount per ml. which will inhibit the growth of a standard strain of *Escherichia coli*, 20 IU being equivalent to 1 μgm. of the pure substance. The authors studied its action on various bacterial species, testing it on many strains of each. It was found to inhibit growth at the following concentrations per ml., results being read after 5 days: *E. coli* 25–100 IU, salmonella 25–100 IU, pasteurella 75–300 IU, Pseudomonas 300–700 IU, *Streptococcus agalactiae* and *equi* 400–1,200 IU. The behaviour of Brucella strains varied, some being inhibited by 100 IU, others resisting 2,000 units, which was the strongest concentration tested. *Br. melitensis* was the most resistant of the genus. *Proteus*, *Str. faecalis*, *Erysipelothrix rhusiopathiae*, and *Bacillus anthracis* also resisted 2,000 units.

E. Agius

LAM, G. T. & SEVAG, M. G. **Inhibitory and Competitive Effects of Sulfathiazole on Transaminases and the Permeability of Sensitive and Resistant** *Staphylococcus aureus*. *Antibiotics & Chemotherapy*. New York. 1959, Apr., v. 9, No. 4, 214–25, 2 figs.

This paper describes a study of transaminase activity in *Staphylococcus aureus* before, during and after acquisition of resistance to sulphathiazole. Measurements of the amount of glutamate produced from alanine, aspartate, leucine and valine all showed diminished activity in the presence of a sub-inhibitory concentration of sulphathiazole, but the activity in the early stages of habituation was restored on transfer to normal medium. When a high degree of resistance had developed, transaminase activities continued to be reduced both in the presence and absence of sulphathiazole, and were not increased, as they had been originally, by the addition of *p*-aminobenzoic acid. Sulphathiazole did not reduce the transaminase activities of cell-free extracts of either sensitive or resistant cells, and these activities were greater in extracts of resistant cells. These findings are considered to mean that the acquisition of resistance to sulphathiazole involves "an altered cell-wall permeability to the reactants of the transaminase system and a compensative acquisition by the internal environment". *L. P. Garrod*

FAZZI, P. L. & DELLA STUA, L. Sull'attività antibatterica della 3-sulfanilamido-6-metossipiridazina e della 3-sulfanilamido-6-cloropiridazina. [**Antibacterial Action of 3-Sulphanylamide-6-Methoxypyridazine and the 3-Sulphanylamide-6-Chlorpyridazine**] *Ann. Sclavo*. Siena. 1959, Mar.–Apr., v. 1, No. 2, 233–44, 6 graphs. [22 refs.] English summary.

This is a study of the *in vitro* activity of 3-sulphanylamide-6-methoxypyridazine, which, being excreted

very slowly, reaches high blood concentrations after low, spaced-out doses, and of 3-sulphanylamide-6-chlorpyridazine which, being eliminated by the kidneys, soon reaches useful concentrations in the urine.

Cultures were carried out on blood agar with concentrations of the sulphonamides ranging from 2,000 to 0·95 μgm./ml. 18-hour broth cultures diluted 1/100 were used as inocula. The activity of the sulphonamides on bacteria in the multiplying phase was studied on *Shigella flexneri*. Growth was observed on a liquid medium to which the sulphonamide had been added in a concentration which had been shown to be, by tests on solid media, the smallest inhibitory dose. Subcultures were carried out on to solid media, 2, 4, 6 and 8 hours after inoculation. Studies on bacterial respiration were carried out with Warburg's apparatus.

Tests were made on 23 strains representing 11 species. The drugs were specially active on *Salmonella* and *Shigella* strains. *Proteus* was also moderately sensitive. None of 6 *Escherichia coli* strains was sensitive to less than 1,000 μgm./ml. while *in vivo* tests show a sensitivity of this species to sulphanylamide-chlorpyridazine. Both drugs appear to have a braking action, rather than a completely bacteriostatic effect, on growing bacterial cultures, a similar effect being also apparent on bacterial respiration. The respiration of cells at rest did not appear to be affected.

E. Agius

Cook, A. M. & Wills, B. A. **The Use of Stored Suspensions of *Escherichia coli* I in the Evaluation of Bactericidal Action.** *J. Applied Bact.* 1958, Dec., v. 21, No. 2, 180–87. [14 refs.]

These authors have previously shown that a suspension of *Escherichia coli* stored at low temperature retains not only viability but a reasonably constant phenol resistance for 2–3 months [this *Bulletin*, 1957, v. 32, 362], and they have suggested that such suspensions might be preferable to young culture prepared by accepted methods for phenol coefficient tests. In this paper they further suggest that such suspensions might be supplied [by whom ?] to laboratories conducting such tests. The further experiments described here show that suspensions in 0·1 M phosphate buffer, *p*H 7·0, are more nearly constant in viable count and phenol resistance than untreated suspensions or suspensions in citrate buffer, and that the degree of loss of resistance during storage was similar for 4 different disinfectants. Expressed as a percentage of the original extinction time after 5 weeks at 4°C. the results were for 1·1% phenol 73·0, 0·66% lysol 63·7, 0·45% Roxenol 66·2, 1·67% potassium laurate 63·5. Some observations were also made on the effects of age of culture, medium and aeration on subsequent viability.

L. P. Garrod

Barwell, C. F. & Freeman, M. A. R. **Sterilisation by Ethylene Oxide.** *Lancet.* 1959, May 2, 917–18.

The objects of these experiments was to investigate the possibility of sterilizing a heart-lung machine with ethylene oxide. No tests were done with the machine itself, but preparations of bacteria in plugged tubes were inserted in lengths of polyvinyl chloride tubing which forms part of the machine in order to study penetrating power. The gas used contained 9% by weight (20% by volume) of ethylene oxide, the remainder being 2 fluorocarbon compounds, "Arcton 6 and 9". The test objects were placed in a McIntosh and Fildes jar without its catalyst, a vacuum of 70–73 cm. Hg was produced and the gas admitted until it reached a pressure of 5 lb. per sq. in. The jar was left for 13 hours at an ambient temperature given as 100–110°F. and the contents were then cultivated. Dried *Bacillus subtilis* spores were killed in 18 out of 19 tests and swabs moistened with a young culture of *Staphylococcus aureus* or *B. anthracis* were killed in all tests. No deleterious effects of the gas were observable on polyvinyl chloride tubing or on acrylic material, but it is remarked that adsorption of ethylene oxide by rubber [this *Bulletin*, 1955, v. 30, 788] and its subsequent liberation during use of the apparatus may prove to be a drawback.

L. P. Garrod

Heman-Ackah, S. M. **The Evaluation of Antiseptic Activities of Solutions of Cetrimide, Iodine, Mercuric Iodide and Chloroxylenol at Different Times after Application to Skins of Africans.** *West African Pharmacist.* London. 1959, Mar., v. 1, No. 1, 3–5, 1 fig.

This paper, from the Department of Pharmacy. Kumasi College of Technology, Kumasi, Ghana, is in the first issue of a journal "devoted to pharmaceutical activities and developments in Nigeria, Ghana, Sierra Leone and Gambia". Its subject is perhaps a little outside this definition. Small areas of the skin on the forearm were treated with 0·2 ml. of antiseptic or 0·2 ml. of sterile water, left to dry for 5, 10, 15, or 20 minutes and then swabbed to remove surplus antiseptic. Pieces of nutrient agar about 1 inch square were applied to these areas for 5 minutes, removed and incubated, after which colonies were counted. The experiment appears to have been done only once, 16 subjects being used, one for each time of drying of each of 4 antiseptics. The colony counts are given in a table and the reduction in count by antiseptic treatment is also presented graphically. Excluding 1 subject whose control culture was uncountable, the average number of colonies from skin treated with water was 23·5 and from that treated with antiseptic 1·5. The best results were given by mercuric iodide 0·1% in 70% alcohol (cultures all sterile after 5 minutes): weak solution of iodine B.P. reduced the count 95–97%, while the results from 0·1% cetrimide and 10% solution of chloroxylenol B.P. were irregular and less satisfactory. [The method is interesting, but many repetitions of such experiments are necessary, and some modifications seem desirable. As the author actually admits, he took no steps to neutralize possible carry-over of mercuric iodide. To determine how much of the apparent efficacy of this solution was due simply to its alcohol content, a test with 70% alcohol alone might with advantage have been included.]

L. P. Garrod

WHITT, Eunice W. **A Surface Film Method of evaluating Quaternary Ammonium Compounds.** *J. Applied Bact.* 1958, Dec., v. 21, No. 2, 272–7. [17 refs.]

This paper is from the Dairy Department, University of Nottingham, and is evidently, although not explicitly, an attempt to define a suitable method for testing disinfectants used in dairying plants. A loopful of *Staphylococcus aureus* culture was spread over one surface of specially cleaned strips of stainless steel, and dried. These were then immersed in a solution of a proprietary disinfectant-detergent in which the former constituent is alkyldimethylbenzylammonium chloride. At intervals a strip was removed, treated with a neutralizer, covered with nutrient agar and incubated: the agar was then peeled off and the colonies on the metal stained with fuchsin and counted. The disinfectant was used in 4 concentrations, equivalent to 200, 150, 100 and 50 p.p.m. of its active constituent, and at 3 temperatures, 58, 100 and 150°F. Percentages of survivors under these conditions at intervals from 15 seconds to 6 minutes are stated in a Table. A kill of 99·5% was given by the recommended concentration, 200 p.p.m. in 2 minutes at all 3 temperatures. Lower concentrations were only effective at higher temperatures, and when 10% of milk was added to the bacterial suspension dried on the strips, 200 p.p.m. gave a satisfactory kill only at the highest temperature. [It is remarkable that bacteria dried on a smooth surface and not fixed in any way should remain there when treated with a solution containing both a quaternary and a detergent. Possibly they did not, and this is a test as much of cleansing as of bactericidal action, but this point is not discussed.]

L. P. Garrod

JENEY, E. & ZSOLNAI, T. Untersuchung der bakteriostatischen Wirkung von Azo-Verbindungen. [**Investigations of the Bacteriostatic Action of Azo Compounds**] *Zent. f. Bakt. I. Abt. Orig.* 1959, v. 175, Nos. 1/2, 133–40. [10 refs.]

Azo compounds known by the proprietary names Pyridium, Urocarmin and Neotropin are administered for infections of the urinary tract. These authors set out to find some better ones, and tested 37 compounds, including 1 of the above named and 7 designated by familiar dye names (chrysoidin, Bismark brown, Congo red, trypan blue, etc.): the full chemical structure of all the compounds is given. The method of test was to determine the minimum inhibitory concentration in broth of *p*H 7·2 for 5 species of bacteria. Most had a moderate or high activity against *Staphylococcus aureus*, a few had slight to moderate activity against *Proteus vulgaris*, and none had any demonstrable activity against *Escherichia coli*, *Pseudomonas pyocyanea* and *Ps. fluorescens*. Since most urinary infections are due to Gram-negative organisms, it is concluded that compounds of this class cannot be expected to influence them. [The authors complain that they could get no information about the bacteriostatic activity of these proprietary compounds except from patent literature. The writer of this abstract tested Pyridium and Neotropin 24 years ago by an *in-vivo—in-vitro* method which has since become standard for this purpose (*St. Bartholomew's Hospital Reports*, 1935, v. 68, 72) and found them devoid of activity as urinary antiseptics.] *L. P. Garrod*

SZITA, J. & BARSY, G. **Studies on the Sporocidal Activity of some Disinfectants.** *Acta Microbiologica.* Budapest. 1959, v. 6, No. 1, 61–6. [12 refs.]

This paper from the State Institute of Hygiene, Budapest, describes tests of the action of 6 disinfectants on the spores of *Bacillus anthracis* and 8 species of *Clostridium*. Silk threads tied in triple loops were used as carriers; these were soaked in 3-day cultures in which sporulation was verified by staining, and dried. The resistance of the spores was tested in HCl and in boiling water [none survived over 40 minutes' boiling and *Cl. tetani* only 10 minutes, which does not seem to surprise the authors as much as might be expected]. The loops were placed in tubes containing 10 ml. of a single concentration of the disinfectant which was kept at 20°C., and removed at intervals varying from 10 minutes to 24 hours and placed in thioglycollate broth (for Clostridia) or a soil extract medium (for *B. anthracis*): if no growth occurred after 1 week they were transferred to a second tube of medium for a further week.

2 of the disinfectants killed all species, 5% formalin in 2–24 hours, and 2% Neomagnol (sodium *p*-toluene sulphonchloramide, to 100 ml. of which 4 ml. of 8% HCl was added) in 0·5 to 8 hours. 5% phenol was ineffective, but when 12% NaCl was added to it *Cl. sporogenes* and *B. anthracis* only were killed in 6 and 24 hours respectively. No effect was obtained with 2% mercury perchloride, 1% Sterogenol (hexadecylpyridinium bromide) or 0·1% Famosept (phenyl mercuric borate).

The immediately succeeding paper is a more detailed study of the action of formalin on *Salmonella typhi* and *Clostridium sordellii*, including a determination of its temperature and concentration coefficients.

L. P. Garrod

KLARMANN, E. G. **Hospital Infection and Environmental Disinfection.** *Soap.* New York. 1959, Feb. & Mar., v. 35, Nos. 2 & 3, 67–70, 104–5; 101–10, 4 figs. [35 refs.]

This paper gives a general account of the principles involved in the use of germicides for purposes of hospital hygiene: it defines terms, discusses testing methods and their deficiencies, and emphasizes that a "disinfectant" must be capable of killing all pathogenic micro-organisms except spores. The problem of staphylococcal sepsis is then discussed, and the mechanisms by which this may be spread. Particular attention is given to 2 preventive aspects, one being the application to floors and other surfaces of a disinfectant with a persistent action in order to reduce the "secondary reservoir" of infection represented by dust particles, the other the chemical disinfection of blankets before laundering. Bacteriological results so obtained are presented, those having reference to

residual surface disinfection being reproduced from the recent paper by DUNKLIN and LESTER [this *Bulletin*, 1959, v. 34, 924]. The disinfectants recommended for these two purposes, Osyl and Amphyl respectively, are manufactured by the Company of whose staff the author is a member. *L. P. Garrod*

SANDIFORD, B. R., BLOWERS, R. & MITCHELL, E. R. **Sluicing of Hospital Linen in Automatic Washing Machines.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1959, June, v. 18, 110–14.

The sluicing by hand of soiled hospital linen is always distasteful, wasteful of time and potentially dangerous. This paper describes tests of an automatic washing machine, made at the request of the General Nursing Council and the Cross-Infection Committee of the Medical Research Council. The machine used was a Bendix Commercial Washer in which two operating cycles were available. In a warm, 1-wash cycle at 32–38°C. a single wash was followed by two rinses and water extraction by spinning. In a hot, 2–wash cycle a first wash and rinse at 32–38°C. were followed by a second wash and rinse at the maximum temperature of the hot-water supply, by 2 more rinses at 49°C. and 32–38°C. respectively and water extraction. The load used was 43–44 soiled infants' napkins, weighing 9 lb. (4 kgm.). Results were assessed by macroscopic examination of the load and machine for faecal matter, by " press-plates " made by pressing the napkins on to the surface of blood agar plates, by swabbing the inside of the drum, and by bacterial counts on the final rinse water. Suitable neutralizers were used when chemical disinfectants had been incorporated in the washing technique.

The 1-wash cycle did not remove visible traces of faecal soiling, even with soap, and was not investigated further. The 2-wash cycle produced moderately satisfactory sluicing without soap and was entirely satisfactory when soap was added. There was no tendency for stains to become fixed in the linen.

The linen and interior of the machine were rendered virtually sterile by using a temperature of 60°C. in the second wash and second rinse, or by adding hypochlorite in a final concentration of 15 p.p.m. chlorine to the final rinse. A quaternary ammonium compound and " several other disinfectants " were not satisfactory.

Slit sampler studies were made of the air near the machine during a low-temperature sluicing run, to see whether a dangerous aerosol was produced. No growth was obtained from 6 samples. The effluent from the early stages of the sluicing cycle was heavily contaminated and the authors suggest that this should be discharged direct to a soil pipe through a trap, or to an outside drain.

It is concluded that the method is satisfactory and safe. If the hot-water supply is at 60°C. no chemical treatment is added, other than soap—at lower temperatures hypochlorite is added.

[See also CRONE, this *Bulletin*, 1958, v. 33, 1167; JERRAM, *ibid.*, 1167.] *J. C. Kelsey*

BOYCOTT, J. A. **The Use of a Washing Machine for Scouring and Disinfecting Babies' Napkins.** *Monthly Bull. Ministry of Health & Pub. Health Lab. Service (directed by Med. Res. Council).* 1959, June, v. 18, 115–16.

In this short note a technique is described for washing and disinfecting babies' napkins in a domestic washing machine fitted with an immersion heater. Washing was done at 80–90°F. (27–32°C.) with a detergent, and took about 10 minutes. The immersion heater was then switched on and the temperature was raised to 180°F. (82°C.), and held for 5 minutes. The original water was then drained away and a final warm rinse was given. This technique produced napkins " at least as clean as when passed through a commercial laundry " and no further washing was needed. Bacteriological tests of the effluent from the washing stage (after heating to 180°F.) and of wringings from the napkins showed no living organisms surviving. The need is stressed for a standardized cycle based on bacteriological experiment, to ensure a heat treatment adequate to kill vegetative bacteria. *J. C. Kelsey*

INDIVIDUAL BACTERIA

In this section the abstracts are arranged as far as possible in the following order:—General; Enteric Organisms; Corynebacterium, Mycobacterium; Staphylococcus; Streptococcus; Brucella; Haemophilus; Pasteurella; Pseudomonas; Neisseria; Donovania; Spirochaetes; Leptospira; Anaerobes; Bacillus; others.

MATTMAN, L. H. & STARNES, R. W. **Sodium Azide in Propagation of L Variants. 1. Variants and the Use of Sodium Azide in their Propagation.** *Yale J. Biol. & Med.* 1959, Apr., v. 31, No. 5, 294–302, 2 figs. on pl. [29 refs.]

The investigation reported here is concerned with devising a method whereby the growth of L variants could be stabilized so that there is no reversion to the bacterial stage and proper *in vitro* studies could be made. Sodium azide is known as a selective inhibitor of Gram-negative bacilli and the studies were confined to *Proteus* organisms, *Salmonella typhimurium* and *Shigella alkalescens*. Sodium azide is active as an inhibitor in concentrations ranging from 0·004–0·0004 M, and in concentrations of less than 0·003 M the swarming of *Proteus* cultures is not inhibited; this would appear to be the critical concentration.

Azide blood agar medium with the azide in this concentration was used for the experiments and it was found that fairly heavy inoculation of this medium in the presence of penicillin (diffusing through the medium) gave a reasonably good yield of L forms. Inoculation of 20,000 or less bacterial cells failed to yield any growth of bacillary or L forms. It would seem therefore that the sodium azide inhibits altogether many organisms that might, under the influence of the

penicillin, make the change to L growth so that the demonstration of L variation requires the bacillary inoculum to be heavy.

Arising out of this observation it has been found that the azide medium is most useful for the isolation of pleuropneumonia-like strains from the cervix or urethra as it largely prevents their overgrowth by the bacillary flora. *H. J. Bensted*

COLOBERT, L. & LOUISOT, P. Formes filtrables d'*Eberthella typhi* obtenues par l'action du lysozyme. [**Filtrable Forms of *Salm. typhi* obtained by means of Lysozyme**] *Ann. Inst. Pasteur.* 1959, July, v. 97, No. 1, 108–11.

Typhoid bacilli exposed to the action of lysozyme in the presence of ethylene-diamine-tetra-acetic acid in a medium without saccharose resulted in the development of forms which will pass through a membrane filter with a porosity of 300–200 mμ. These filtrable forms can regenerate into normal bacillary forms in a few hours if subcultured into a nutrient broth medium containing 0·3 M. sucrose plus 20% serum.

It is suggested that these filtrable forms may be identical with the salmonella "polar granules" which appear to be about the same size and which are considered by many workers to be bacterially nuclei.

[See also this *Bulletin*, 1959, v. 34, 269.]

H. J. Bensted

VASSILIADIS, P. Diagnostic sérologique de *S. typhi* isolés par hémocultures. Quelques remarques sur ces hémocultures. [**Serological Diagnosis of *Salmonella typhi* Isolated by Bloodculture and Observations on the Methods of Culture**] *Ann. Soc. Belge de Méd. Trop.* 1957, Oct. 31, v. 37, No. 5, 743–7.

This is an account of the serological identification of 140 strains of typhoid bacilli isolated from blood cultures. Preliminary examination was by slide agglutination tests of living cultures with pure TVi and pure TO sera. All the cultures were agglutinated by the Vi serum, but the agglutinability with the O serum was variable—some of the cultures showed little or no agglutination. When tubes of suspensions of the cultures were heated to 85–90°C. for 20 minutes satisfactory O-agglutination was obtained in every case. After heating many of the cultures failed to show any Vi-agglutination and the remainder reacted poorly with Vi serum. In the preparation of anti-Vi agglutinating sera the author found that higher titres were obtained with sera prepared from goats than with those from rabbits.

In discussing the merits of bile and nutrient broth as media for blood culture for the diagnosis of typhoid fever the experience of the author favoured bile. In 250 positive blood cultures done in parallel in bile and broth 9% were positive only in the bile cultures and 4% were positive only in the broth, otherwise there was agreement. *H. J. Bensted*

SERVANT, Paule, REY, L. & BONÉT-MAURY, P. Contribution à l'étude des conditions de conservation de la viabilité d'une souche de bacille typhique par lyophilisation en vue de la fabrication d'un vaccin radio-inactivé. I.—Étude de la phase de congélation initiale: recherches sur la résistance du bacille typhique à l'exposition aux basses températures. [**Preservation of Viability of a *Salmonella* Strain by means of Freeze-Drying with a View to the Production of a Radio-Inactivated Living Vaccine. I.—Study of the Initial Freezing Phase. Resistance of Typhoid Bacillus to Low Temperatures**] *Ann. Inst. Pasteur.* 1959, June, v. 96, No. 6, 755–64, 2 figs. [34 refs.]

In studying various techniques for the preparatory low temperature-treatment of bacterial cultures before lyophilization the authors found, in common with other workers, that the ultimate viability of the organisms concerned was influenced by the medium used for suspending the culture, the actual temperatures and methods used for the quick freezing and the period of exposure to these temperatures.

With the typhoid bacillus it was found that of the various suspending media tried, 10% glucose in distilled water gave the best results. Cultures suspended in this medium should be exposed in thin layers—such as are obtained with small quantities of suspension in a tube when it is rapidly rotated in a vertical or near vertical plane—to temperatures of − 30°C. or less for periods of about 10 minutes. By this method very rapid freezing of the culture is obtained and a reasonably high degree of viability assured. The authors consider that this preliminary treatment enables suitable dried cultures to be prepared for their subsequent experiments with cobalt rays. *H. J. Bensted*

SPAUN, J. **Typhoid Vaccine. Vi Antigen and Vi Antibody.** *Acta Path. et Microb. Scandinavica.* 1957, Suppl. 123, 79 pp. [Numerous refs.]

Dr. Spaun is a member of the staff of the State Serum Institute in Copenhagen and he has been interested in the Vi antigen of the typhoid bacillus since 1951. He is known for his development, independently of LANDY, of the Vi-haemagglutination test, a valuable tool for the estimation of Vi antibody. This volume does not present any new knowledge but is more in the nature of a critical review of the experimental work designed for the determination of the properties of the Vi antigen, the examination of the role of Vi antibody in immunity studies of typhoid fever when the mouse is used as the experimental animal, and the interpretation of these results in relation to the natural infection. Much has been written about the fundamental difference between the natural infection, which is restricted to man, and the condition produced by injecting living typhoid bacilli into the peritoneum of the mouse. The mouse is not susceptible to infection by the typhoid bacillus. Whereas 10, or even one bacterial cell, *Salmonella typhi-murium*, injected into a mouse can set up a progressive infection during which the organism continues to multiply until

the total bacterial population—just before the death of the animal—reaches a figure of about 10^9 there is no evidence to show that a simple suspension (that is without mucin, for instance) of typhoid bacilli injected into the peritoneum of a mouse ever multiplies. The injection results in antibody response when sub-lethal doses are given but the organisms, which are to be found in most of the tissues, are gradually eliminated and it is only when the appropriate dose (varying from 500×10^6 to 50×10^6, according to the culture used) is injected that deaths result within 18–48 hours.

The author suggests that there is no basis for regarding the Vi antigen content of the culture being responsible for the variation in the LD50 for mice which may be found with different cultures. While this may be true to some extent with Vi variants of typhoid bacilli deficient in O antigen, and with other bacterial types carrying the Vi antigen, there is a mass of evidence to support the view that, with typhoid bacilli with a full complement of O antigen, mouse-virulence is directly proportional to the Vi content of the culture. It is quite obvious in the papers of FELIX and others what these authors meant when they produced this evidence and it is equally obvious that they were well aware that without the O antigen of *Salm. typhi* (or some undefined factor in the antigen complex) the Vi antigen behaved differently.

This type of argument, of which the above example is not unique, seems unnecessary and unhelpful. There are some mis-statements in connexion with the use by the British Army of alcoholized TAB vaccine which appear to be due to misunderstandings and are not unreasonable. Stimulated undoubtedly by Felix's work on the alcoholized vaccine, but quite independent of Felix himself, Army pathologists carried out a long series of experiments and trials during the war with the new vaccine and it was only when the results fully confirmed Felix's findings that it was decided in 1944 to change over from the heat-killed phenol-preserved vaccine to the alcoholized preparation but to retain the Rejuvenated Rawlings (not "Rawling" as printed in this book) strain as the typhoid element—strain Ty 2 was introduced much later. Mainly owing to administrative difficulties and the existing stocks of the older vaccine, comparatively few troops were inoculated with the alcoholized vaccine before the end of the War. BOYD's paper in 1943 [this *Bulletin*, 1943, v. 18, 704] about the inoculation of prisoners of war with British Army vaccine clearly referred to the heat-killed phenol-preserved preparation and he certainly never expressed the opinion that the alcoholized vaccine was the best prophylactic.

Although there is no doubt about the immunological value of the Vi antigen in protecting mice against a subsequent challenge with virulent typhoid bacilli, the translation of these findings to the protection of man against typhoid fever by immunological procedures is almost as far away as it was 60 years ago. The early extravagant claims of the value of bacterial vaccines as prophylactics against human infections may have been based on premises which have been shown to be not altogether sound and this little monograph certainly illustrates some of the difficulties that confront the practical immunologist to-day. *H. J. Bensted*

BUONOMINI, G. & GABRIELLI, G. Il problema del controllo dei vaccini antitifici. Nota II. Prove comparative tra i vari metodi proposti per valutare la efficacia di un vaccino. [**The problem of control of Typhoid Vaccines. II. Comparative Tests of the Various Methods Suggested for evaluating the Efficacy of a Vaccine**] *Ann. Sclavo.* Siena. 1959, Mar.–Apr., v. 1, No. 2, 151–62. [16 refs.] English summary.

For comparative purposes use was made of methods depending on active immunization of white mice, of the production of antibodies in rabbits, and of passive immunity tests in white mice and on chick embryos. Formolized and alcoholized vaccines were used, mucin was used in one set of tests and not in another, one infecting dose was used in one set and a series of doses in another. *Salmonella typhi* Ty. 2 served throughout as the vaccine strain and as the infecting agent.

An active immunity test which was studied was that described by BONET-MAURY *et al.* [see this *Bulletin*, 1954, v. 29, 863]. White mice were inoculated intramuscularly with a vaccine dose of 300 million bacteria and infected after a 10-day period with repeated doses intraperitoneally. Results, plotted on log-probability paper, gave an index of efficacy of the vaccine. 2 passive immunity tests were tried. Rabbit immune sera were inoculated in 1 ml. doses intramuscularly in 50 white mice which 48 hours later were given intraperitoneally 0·5 ml. of a suspension containing 600 million typhoid micro-organisms. In the chick embryo, following the GRABAR and LE MINOR technique [this *Bulletin*, 1952, v. 27, 367] as modified by Gabrielli (who adopts inoculation in the allantoic cavity), the serum under test, diluted 1 in 10, was mixed with an equal volume of bacterial suspension containing 200, 2,000 and 20,000 bacteria per ml. Results were read after 48 hours' incubation at 37°C.

The use of mucin was found not only to decrease the survival rate but to interfere with the assessment of differences between the various types of vaccines: blocking humoral defences, it interferes too drastically with the immunity processes under study. Active immunity tests on mice stretch over so long a period (7 weeks at least) that other factors may disturb the result. The test of Bonet-Maury *et al.* has great advantages. The rabbit antibody response was found unsuitable for assessing the protective power of a vaccine. Rabbit immunization could only be useful in preparing sera to be used in passive protection tests, which can be carried out on white mice, or, preferably on chick embryos. In conclusion it is clear that active and passive immunization tests on mice, and tests on chick embryos give highly significant results, the simultaneous use of the 3 methods certainly making possible an objective estimation of the value of a vaccine. For practical purposes active immunity mice tests are more than enough, while the chick embryo test is more useful in human cases where less serum may be available. *E. Agius*

STOKES, J. L. & BAYNE, H. G. **Growth-Factor-Dependent Strains of Salmonellae.** *J. Bacteriology.* 1958, Oct., v. 76, No. 4, 417–21. [13 refs.]

The authors selected 4 cultures, *Salmonella typhi-suis*, *Salm. abortus ovis*, *Salm. paratyphi A* and *Salm. fulica*, and examined their growth requirements with a chemically defined medium to which were added various amino-acids, vitamins and purines. The basic medium was composed of glucose 1% $(NH_4)_2SO_4$–0·1%, Na citrate.$2H_2O$–0·05%, $MgSO_4.7H_2O$–0·05%, and phosphate buffer *p*H 7·1–0·05 M. The organisms under test would not grow on the basic medium alone. The purines, adenine or guanine, appeared to be interchangeable, but the need for vitamins, thiamine or nicotinic acid was an individual requirement. With regard to the amino acids, cystine was always essential but in order to obtain optimum growth other amino acids might be necessary and each had to be tested. Ordinary laboratory culture media often lacked cystine because during the preparation of such media it was either destroyed or made unavailable. *H. J. Bensted*

JOACHIN, Alicia, MAYES, Otila & OLARTE, J. **Sensitivity of *Salmonella* Species to Synnematin B, Chloramphenicol, and Tetracyclines. A Study of One Hundred Ten Freshly Isolated Strains.** *Antibiotics & Chemotherapy.* New York. 1959, June, v. 9, No. 6, 349–52, 1 fig.

These authors from Mexico City collected 32 strains of *Salmonella typhi-murium*, 24 of *Salm. oranienburg* and smaller numbers of other species to a total of 110 (including 3 of *Salm. paratyphi* B but no *Salm. typhi* or *Salm. paratyphi A*) and tested their sensitivity to antibiotics by a plate dilution method. All 3 tetracyclines were included, but results did not differ significantly and only those for tetracycline are given. Most strains were inhibited by 0·6 or 1·2 μgm./ml. of this antibiotic, and 7% were resistant. Corresponding figures for the other 2 antibiotics studied were: chloramphenicol 2·5 or 5 μgm./ml., 1% resistant: Synnematin B 0·5, 1 or 2 μgm./ml., 4% resistant. There was no evident relationship between species and degree of sensitivity. *L. P. Garrod*

BÖHME, D. H., SCHNEIDER, H. A. & LEE, Johanna M. **Some Physiopathological Parameters of Natural Resistance to Infection in Murine Salmonellosis.** *J. Exper. Med.* 1959, July 1, v. 110, No. 1, 9–26, 4 text figs. & 23 figs. on 6 pls. [31 refs.]

In these studies 2 inbred mouse-strains were used: one, BSVS which is susceptible to *Salmonella typhi-murium*, the other BSVR which is resistant to mouse typhoid. Mice were infected by the double-strain inoculation procedure, with the RIA, avirulent, and the SR 11, virulent, strains of *Salm. typhi-murium*. When comparable batches of BSVS and BSVR were inoculated by this procedure all the BSVS mice died and 52% of the BSVR mice survived.

There was no pre-infection difference in the activity of the reticulo-endothelial system (RES) of the BSVS and BSVR mice and after infection the increases in RES activity were of about the same magnitude in the 2 groups, but there was a difference in the time of onset. Susceptible animals showed an early short increase in RES activity followed by a drop to control levels at the time of death. Resistant animals showed a delayed RES reaction, but the activity was very significant and this did not return to normal levels until some 4 weeks after infection.

Changes in the liver and spleen occurred earlier in the BSVS mice than in the BSVR mice; in the resistant animals the livers were almost free by the 22nd day of abnormal appearances. Focal necroses having disappeared. Nevertheless these BSVR mice, although apparently healthy, remained carriers of *Salm. typhi-murium* for the rest of their lives [this *Bulletin*, 1958, v. 33, 65]. *H. J. Bensted*

STOCKER, B. A. D. & CAMPBELL, Janet C. **The Effect of Non-Lethal Deflagellation on Bacterial Motility and Observations on Flagellar Regeneration.** *J. General Microbiol.* 1959, June, v. 20, No. 3, 670–85, 1 fig. [33 refs.]

During their studies on the genetics of motility and flagellation in salmonella organisms the authors investigated a number of possible methods of removing flagella from bacteria without loss of viability. There is no satisfactory method of stripping selected individual bacteria of their flagella, but whole cultures were non-lethally deflagellated by acid treatment or by mechanical methods. The satisfactory chemical treatment was a development from DUNCAN's original observations [this *Bulletin*, 1936, v. 11, 70] on the effect of weak mineral acids on the H-antigen. Dense suspensions of *Salmonella typhi-murium* cultures were added to citrate + phosphate buffers of nominal *p*H values ranging from 2·4 to 3·0 and the exposure treatment terminated after ½, 1 or 2 minutes by the addition of a large excess of neutral buffer. It was found that while this treatment did not significantly affect the viability, the proportion of flagellated organisms was reduced from about 64% to less than 1%.

Although there are several mechanical methods of deflagellating bacteria for the production of pure flagellar suspensions most of these were not suitable for the purpose of this study; 2 were, however, highly successful. Rubbing the bacterial growth on stiffish nutrient agar (New Zealand agar 3%) with an angled glass rod deflagellated more than 90% of the organisms without significantly affecting the viability; the second method utilized the violent "stirring" action obtained with a MSE [Measuring and Scientific Equipment, Ltd.] blendor to produce almost complete deflagellation without detectably reducing the viable count.

Very small numbers of bacteria retained their motility after the acid treatment, presumably because of acid resistance of their flagella. Further investigation of this phenomenon with appropriate single cell isolations indicated, however, that such bacteria were not in fact mutants with acid-tolerant flagella. It seems fairly clear that bacteria that remain motile after the rubbing treatment do so because, by chance, they have escaped proper contact with the glass rubber and not because of any peculiar resistance to deflagellation.

The quantitative aspect of deflagellation was checked by microscopic examination of stained preparations by phase-contrast illumination and of moist preparations by dark-field illumination. Many of the observations made are of great interest. For instance the results of blending treatment suggests that this method removes flagella by repeated breaking-off of their distal parts rather than shearing them off at the base. It would seem that the critical length of a flagellum is about 2·9μ. When the majority of the flagella on a bacterium are longer than this translational movement occurs; when below this figure only rotational motility is noted. Serological tests on washed bacteria, deflagellated by blending, confirmed that the H-antigen was present only in the flagella. Experiments on the regeneration of flagella indicate that they are not suddenly extruded as fully formed appendages, but grow slowly, gradually elongating over a period and thereafter persist for many generations without further elongation. At the same time deflagellation does not affect the rate of growth of flagella; it is quite probable that this is controlled from the base. *H. J. Bensted*

RAETTIG, H. Provokation einer Infektion durch Schutzimpfung. I. Mitteilung. Spezifische Provokation während der experimentellen Epidemie mit *S. typhi murium*. **[Provocation of an Infection by Vaccination. I. Specific Provocation during an Experimental Epidemic of** *S. typhi-murium***]** *Zent f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 3/4, 192–217, 10 figs.

In the course of the very heavy epidemic of typhoid fever which occurred in Vorpommern and Mecklenburg in the summer of 1945, the suspicion arose that prophylactic vaccination which coincided with the incubation period of the disease was responsible for increase in the severity of the cases [this *Bulletin*, 1951, v. 26, 1059].

In view of this, an experimental investigation has been carried on over several years on the effect of subcutaneous inoculation of mice with killed bacterial vaccine at an interval of about a week after they had been given a suspension, 10^8 bacteria/ml., of a mouse typhoid strain to drink when thirsty. Many batches of mice, varying in size from 9 to 316, were thus tested, and both strains of varying virulence and groups of mice of varying resistance were used. In all, several thousand mice were used.

Apart from one or two experiments in which highly sensitive breeds of mice were fed with strains of unusual virulence, the epidemics produced were more severe in the vaccinated animals, *i.e.* there were earlier deaths and a greater total mortality.

The types of curve characteristic of the "natural" epidemic—mice infected only—and of the "provoked" epidemic—mice infected and vaccinated—are presented.

It is suggested that some recorded human epidemics have shown curves of the type described for a "provoked" epidemic (*Provokationsepidemie*). Thus the curve of poliomyelitis in Chicago in the first year of vaccination, 1956, contrasts with a curve based on the epidemics of previous years, in much the same way as the author's experimental and control mouse typhoid epidemic curves. *J. W. McLeod*

DEMEREC, M. & OZEKI, H. **Tests for Allelism among Auxotrophs of** *Salmonella typhimurium*. *Genetics.* 1959, Mar., v. 44, No. 2, 269–78. [18 refs.]

VAN OYE, E., LUCASSE, C. & VAN GOETHEM, H. Note sur une série d'infections provoquées par une *Salmonella enteritidis* ayant des caractères biochimiques non conformes. **[A Series of Infections due to a Biochemically Atypical Strain of** *Salm. enteritidis***]** *Ann. Soc. Belge de Méd. Trop.* 1959, Feb. 28, v. 39, No. 1, 123–7.

This is an account of a small outbreak in which an atypical *Salmonella enteritidis* was isolated from the blood and faeces of 7 adults and 3 infants. The organism had the typical antigenic characters of its serotype, but the biochemical characters were unusual in that all the cultures isolated fermented salicin, with the production of acid and gas, in 36 hours.

H. J. Bensted

OKONOGI, T., FUKAI, K., MITSUHASHI, S., NAGAI, M. & KAWAKAMI, M. **Studies on the Experimental Typhoid. III. Histopathological Study of the Mice Liver infected with Virulent or Attenuated** *S. enteritidis* **Strain.** *Japanese J. Exper. Med.* 1959, Apr., v. 29, No. 2, 71–7, 10 figs. on 5 pls. [44 refs.]

Salmonella enteritidis infections in mice are considered to imitate the histopathological picture seen in the livers of human cases of typhoid fever and this paper is concerned with the changes seen in mouse livers after infection with virulent and attenuated strains of the living organisms and also with the changes seen in the liver after the injection of killed suspensions of *Salm. enteritidis*. Virulent living cultures regularly killed the mice within 6 days and the livers showed multiple abscess formation. The abscesses were roundish in shape filled with necrotic material. With the attenuated strain small irregular-shaped nodules were found after about a week and the histological picture showed a general reticulo-endotheliosis together with a number of focal necroses, not rounded as seen in the acute condition with the virulent strain. Mice injected with the killed enteritidis vaccine showed at 2 weeks a definite cellular reaction in the glandular tissue of the liver with dilated sinusoids filled with Kupffer cells, epithelioid and mononuclear cells. Later on fatty changes were seen in the liver cells.

[It seems doubtful if experimental studies of this sort add greatly to our knowledge of the early changes that occur in the liver of patients suffering from typhoid fever, but it is of interest to know that experimental typhoid in the mouse produces a pathological picture of the same order in the liver as that seen in the natural human disease. It would seem, however, that the progress of *Salm. enteritidis* infections in mice, even with attenuated strains, is so rapid that it is difficult to obtain material that shows the very early stages of focal necrosis in the liver which were so accurately described by pathologists nearly 50 years

ago with regard to the human liver when typhoid fever was a very common disease.] *H. J. Bensted*

KUWAHARA, S., YASUSHI, S., OWA, T. & SHINODA, M. **Nutrition of *Salmonella pullorum* and *Salmonella gallinarum*. I. Growth Factor and Amino Acid Requirements.** *Japanese J. Microbiol.* 1958, Oct., v. 2, No. 4, 343–9.

"Comparing 15 strains of *Salmonella pullorum* and 11 strains of *Salmonella gallinarum* in nutritional requirements the following results were obtained.

"1. Three strains of *S. pullorum* and 6 strains of *S. gallinarum* did not require any growth factors, but of the other strains, a combination of 3 vitamins—niacin, thiamine and riboflavin—was necessary for growth.

"2. By an elimination test a medium containing 7 amino acids—glycine, asparagine, glutamic acid, proline, cystine, arginine and tryptophan—was found to support a moderate growth of all tested strains.

"3. *S. pullorum* is more exacting than *S. gallinarum* in both growth factor and amino acid requirement (proline, glutamic acid and cystine)."

GÁSPÁR, G. **Correlations between the Antigenic Structure and Phage Sensitivity of Types of Group *Shigella flexneri*.** *Acta Microbiologica.* Budapest. 1958, v. 5, No. 3, 243–51.

A remarkably close correlation has been demonstrated by the author between the antigenic and phage types of the Flexner group of dysentery bacilli. 10 Flexner phages have been identified and these with few exceptions correspond to specific antigen types. Thus *Shigella flexneri* 1a = phage *a*, 1b = *b*, 2a = *c*, 3 = *d*, 4a = *e*, 4b = *f*, 6 = *g*, 6 = *h*, 2b and X = *i*, and 4a and Y = *k*. It will be seen the correlation is not quite complete, but it is of considerable interest to note that *Sh. flexneri* 2b shares phage *i* with the X-complex and that 4a shares phage *k* with the Y-complex. *Sh. flexneri* 6 is sensitive to either phage *g* or to phage *h*, but this different sensitivity appears to have no relation to the three biochemical types: Newcastle, Manchester or Boyd 88. Other pathogenic groups among the Enterobacteriaceae have been tested against these phages; a few show slight evidence of sensitivity but the majority are resistant.

The method of classifying members of the Flexner group according to their phage sensitivity has often been considered, but it seemed to offer no advantages over the serological method unless there was any evidence to show that non-Flexner organisms, known to be antigenically related, were insensitive to these phages. Highly absorbed type sera are very simple to use and identification by experienced workers can be effected very rapidly by the serological method for the detection of the specific antigens. It does not appear that phage sensitivity is a more accurate epidemiological tool than antigenic identification, but further investigation may well show finer divisions in the antigenic types.

H. J. Bensted

RAUSS, K., KÉTYI, I., RÉTHY, L. & JOÓ, I. **The Significance of the Inoculation Interval in Vaccination with Polyvalent Dysentery and Combined Typhoid-Dysentery-Tetanus Vaccines.** *Acta Microbiologica.* Budapest. 1959, v. 6, No. 1, 51–9. [17 refs.]

The authors in some pilot experiments with a Boivin type extract of *Shigella flexneri* 2a (a prevalent type in Hungary) as a vaccine for 2-dose immunization of mice evaluated by active protection tests, found that a 2-weeks interval between the doses gave better results than 1 week. Increasing the interval to 4 weeks gave results of the same order. In the human trials with a polyvalent dysentery vaccine adsorbed onto an alum precipitate the post-inoculation sera were examined by the passive protection test in mice and it was found that, whereas increasing the interval between the two doses from 2 to 4 weeks gave significantly better protection, as measured by the passive test in mice, a further increase to 6 weeks seemed to be of little advantage. However, in another series with spaced intervals from 3 to 6 weeks the longer interval gave the better results.

The trials with the typhoid-dysentery-tetanus prophylactic showed that the increase of the interval between the two doses from 4 to 6 or 8 weeks greatly improved the protection afforded. Moreover, the groups showing low levels of antibody with the 4-week interval disappeared altogether when the interval was increased to 8 weeks. *H. J. Bensted*

KÉTYI, I. **Intracutaneous Administration of Dysentery Vaccine.** *Acta Microbiologica.* Budapest. 1958, v. 5, No. 3, 271–7, 1 graph. [18 refs.]

Shigella vaccines given intradermally to rabbits were compared with similar vaccines (Boivin extracts or bacterial suspensions) given subcutaneously. Sera from these immunized animals were put up in parallel in passive mouse protection tests and sera from the intradermally immunized rabbits were found to have greater protective value.

Results of the same order were obtained with tests in man, but it was found that the intradermal vaccines caused local necrosis at the injection site and it was decided that the method was not suitable for application to man. *H. J. Bensted*

SPICER, C. C. **The Survival of *Shigella sonnei* on Cotton Threads.** *J. Hygiene.* 1959, June, v. 57, No. 2, 210–15, 3 figs.

Although the dysentery bacillus of Sonne is commonly regarded as a resistant organism on the grounds that it can be so frequently isolated from dysenteric exudates that have stood on the bench for several days, as far as is known this is the first account of fully controlled quantitative experiments to determine the survival of *Shigella sonnei* when allowed to dry from pure suspensions in broth and double glass-distilled water under different conditions of relative humidity and temperature.

Ordinary cotton thread which had been well washed in, and then subsequently boiled for half an hour in distilled water to remove the size and any toxic substance, was cut up into lengths of 4". These threads

served as the material on which the tests were made; they were attached in groups of 20 to lengths of wire by which they could be suspended in closed screw-capped jars and exposed to different relative humidities (0–84%) by placing saturated solutions of various salts in the body of the jars. (This ingenious apparatus was described in a report by the Committee on Formaldehyde Disinfection, this *Bulletin*, 1959, v. 34, 477.) The hanks of thread were soaked in suspensions of *Sh. sonnei* of determined bacterial concentrations and, with due precautions, exposed to the different conditions over various periods of time after which the survival rates were estimated.

It was found that with relative humidities between 40 and 60% the survival rates were much lower than when the percentage was well below or well above these figures. Survival was better at low temperatures (5–10°C.) than at temperatures of 20–30°C. Under favourable conditions viable *Sh. sonnei* could be recovered from the cotton threads after 10 days. The minimum of survival at intermediate RH (50%) with broth suspensions of *Sh. sonnei* appeared to be similar to the results of the experiments on the survival of airborne suspensions of pneumococci in droplets [Dunklin, E. W. & Puck, T. T., *ibid.*, 1948, v. 23, 347] but whereas these authors reported that this minimum was abolished when the suspensions were made in distilled water instead of broth, Spicer (who took the precaution of using doubled-distilled water from a glass still) was unable to confirm this effect for *Sh. sonnei*. Indeed his results were very consistent and fully confirmed his previous observations regarding the minimum survival of *Sh. sonnei* in a relative humidity of about 50%. No satisfactory explanation can be offered for this interesting result. In comparing this fully controlled scientific experiment with the casual tests done on stools from acute cases of Sonne dysentery it must be appreciated that the presence of large amounts of mucus with almost pure cultures of *Sh. sonnei* might well result in a much prolonged survival of the infecting organism. *H. J. Bensted*

Coetzee, J. N. **The Mutation Rate of Phase I** *Shigella sonnei* **to Phase II.** *South African J. Lab. & Clin. Med.* 1959, Mar., v. 5, No. 1, 29–38, 4 figs. [17 refs.]

"A fluctuation test was performed, which supports the mutational origin of phase-II from phase-I *Shigella sonnei*.

"By means of continuous culture experiments, this mutation rate was estimated to be $6{\cdot}3 \times 10^{-4}$/bacterium/generation. Under conditions prevailing in these experiments, the back mutation rate was zero."

Fleischhauer, G. Über einen Toxinnachweis bei Colibakterien mit Hilfe einer Präzipitinreaktion. II. Mitteilung. [**The Demonstration of** *E. coli* **Toxin with the Agar Gel Diffusion Test. 2nd Communication**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 5/6, 388–94, 7 figs.

The English summary appended to the paper is as follows:—

"Precipitation lines can be demonstrated in agar gel diffusion tests when E. coli strains and their homologous sera are used. Studying the interference of such precipitation lines, produced by living and dead colonies and pure endotoxins, it could be shown that the precipitation is chiefly produced by liberated endotoxins. Heating at 100°C. for 60 minutes considerably diminishes the precipitation. E. coli cells killed by formaldehyde (one percent for 4 hours) do not cause poorer precipitation lines. With this method exotoxins could not be demonstrated in dyspepsia coli strains."

Meadow, Pauline & Work, Elizabeth. **Biosynthesis of Diaminopimelic Acid and Lysine in** *Escherichia coli.* **1. The Incorporation of 14C from Various Organic Precursors into the Diaminopimelic Acid of a Lysine-Requiring Mutant.** *Biochem. J.* 1959 July, v. 72, No. 3, 396–400. [24 refs.] **2. Incorporation of [14C] Diaminopimelic Acid, Lysine and Glucose.** *Ibid.*, 400–407. [21 refs.]

McFall, Elizabeth & Stent, G. S. **Continuous Synthesis of Deoxyribonucleic Acid in** *Escherichia coli. Biochim. et Biophys. Acta.* 1959, Aug., v. 34, No. 2, 580–82, 1 fig.

Bowen, T. J., Dagley, S. & Sykes, J. **A Ribonucleoprotein Component of** *Escherichia coli. Biochem. J.* 1959, July, v. 72, No. 3, 419–25, 2 figs. [40 refs.]

Scott, D. B. McN. & Chu, Eileen. **The Oxidative Pathway of Carbohydrate Metabolism in** *Escherichia coli.* **6. Adaptation of Glucose 6-Phosphate Dehydrogenase to Growth in Complex Media.** *Biochem. J.* 1959, July, v. 72, No. 3, 426–9, 1 fig. [10 refs.]

Countryman, Joan L. & Volkin, E. **Nucleic Acid Metabolism and Ribonucleic Acid Heterogeneity in** *Escherichia coli. J. Bacteriology.* 1959, July, v. 78, No. 1, 41–8, 3 figs. [21 refs.]

Weinbaum, G. & Mallette, M. F. **Enzyme Biosynthesis in** *Escherichia coli. J. General Physiol.* 1959, July 20, v. 42, No. 6, 1207–18, 2 figs. [27 refs.]

Kanazir, D., Barner, Hazel D., Flaks, J. G. & Cohen, S. S. **Some Physiological and Genetic Properties of a Strain of** *Escherichia coli* **requiring Thymine, Arginine and Uracil.** *Biochim. et Biophys. Acta.* 1959, Aug., v. 34, No. 3, 341–53, 2 figs. [21 refs.]

Yaoi, H., Nakamura, W. & Tomino, H. **Promoting Effect of Vaccinia Virus (PVL) on Nucleic Acid Synthesis of** *Escherichia coli. Yokohama Med. Bull.* 1959, June, v. 10, No. 3, 131–9, 8 figs.

KRATOCHVÍL, I, TARABCÁK, M & BAUER, W. Epidemiologický význam *E. alcalescens.* [**Epidemiologic Significance of** *E. alcalescens*] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1959, v. 8, No. 4, 245–50, 1 graph. [12 refs.]

The English summary appended to the paper is as follows:—

"Observations of 204 cases of diarrhoetic disease are being reported, of which 110 arose as an epidemic outbreak in an isolated collective. Etiological agent of the diseases were germs of the group alcalescens-dispar detected by epidemiologic, clinical, cultivational and serologic observations. 33 strains were isolated from adults in sporadic cases of dysenteriform diseases. 17 strains come from sporadic cases of infantile dyspepsies, one of which ended lethally. 44 cases are accidental isolations from the stools of healthy persons without clinical symptoms.

"Epidemiologic significance of E. alcalescens is being discussed. A view is being proved that the germs of the group alcalescens-dispar are conditionally pathogenic."

DUBAY, L. K otázke biochemických vlastností Klebsiely typu 4 (Ozaenae). [**On the Question of Biochemical Properties of** *Klebsiella,* **Type 4 (Ozaenae)**] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1959, v. 8, No. 4, 235–8. [11 refs.]

The English summary appended to the paper is as follows:—

"On the grounds of an investigation of biochemical properties of 150 strains of Klebsielle, Type 4 [ozaenae] we have come to the conclusion that unambiguously positive results are obtained by following tests: fermentation of adonite, of mannite, of raffinose and glucose in 24 hours, exceptionally in 48 till 72 hours. A test based on the consumption of ammonium citrate as the only source of organic carbon as well as the methyl red test gave positive results, with only a few exceptions, too.

"Not even one strain fermented dulcit within 30 days. Negative results without any exception were obtained by following tests: formation of indole, formation of H_2S liquefaction of gelatin. Voges-Proskauer test as well as urease test [read after 4 days] except for a few isolated cases were also negative.

"Carbohydrates, as arabinose, ramnose, maltose, lactose, saccharose and sorbose are fermented by many strains in various time intervals up to 30 days. By a certain number of strains they are not changed even after this interval."

FULTON, M., FORNEY, Clare E. & LEIFSON, E. **Identification of Serratia occurring in Man and Animals.** *Canadian J. Microbiol.* Ottawa. 1959, June, v. 5, No. 3, 269–75, 7 figs. on pl. [36 refs.]

Serratia marcescens (*Chromobacterium prodigiosum*) has occasionally been isolated from clinical material. As it may pass unrecognized or be diagnosed as a "paracolon" (pigment may not be shown on ordinary media) its significance is doubtful. Chance restoration of pigment to a "paracolon" led to the examination of 21 strains from which other characters were found to identify non-pigmented strains.

In morphology 18 strains had peritrichous flagella with characteristic coils; one strain, ATCC 4002 [not NCTC 4002 as stated] showed two types, one with coiled, the other with wavy flagella; both bred true, and in all other respects the types were indistinguishable.

Biochemical tests suggested two patterns of reactions with differences in the following tests: adonitol, arabinose, dextrin, gas from glucose, lactose, lactose slant [increased lactose concentration], melezitose, melibiose, methyl glucoside, raffinose, xylose and gelatin,

While the flagella shape is characteristic, unpigmented cultures may be recognized by the following set of characteristics: anaerogenic, H_2S-negative, acid from maltose, mannitol, salicin and sucrose, while no change occurs in xylose. *S. T. Cowan*

HUGH, R. **Oxytoca Group Organisms isolated from the Oropharyngeal Region.** *Canadian J. Microbiol.* Ottawa. 1959, June, v. 5, No. 3, 251–4. [14 refs.]

LAUTRUP (*Acta. Path. et Microb. Scandinavica,* 1956, v. 39, 375) suggested the name [not epithet] *Klebsiella oxytoca* for a group of non-motile, indole +, gelatin-liquefying coliforms. Hugh collected 19 such strains, 15 from the oropharynx and 4 from faeces. All strains fermented a large number of sugars [including adonitol which is more or less specific for *Klebsiella*] with the production of acid and gas, and were positive in the following tests: indole, V-P, citrate, KCN, nitrate reduction, catalase, lysine decarboxylase. They were non-motile, did not produce H_2S or reduce nitrite and were phenylalanine negative. Variable results were given in a few tests: MR (8 +, 8 −, 3±); dulcitol (9 +, 10 −); gelatin (15 +, 4 −); urea (18 +, 1 −).

The author would remove the Oxytoca [capital O] group from *Klebsiella* and from a heterogeneous "intermediate" [not equivalent to Intermediate coliforms of English bacteriologists = *Citrobacter freundii*] group of PARR (*Bact. Reviews,* 1939, v. 3, 1), but would not perpetuate "the error of past classifications" by using a species name for it. *S. T. Cowan*

SOUCEK, A. & NOVOTNÝ, P. Návrh metodiky pro rutinní vyšetřování *Corynebacterium diphtheriae.* [**Proposing a Method for Routine Examination of** *Corynebacterium diphtheriae*] *Československ. Epidemiol., Mikrobiol., Imunol.* Prague. 1959, v. 8, No. 4, 217–27. [14 refs.]

The English summary appended to the paper is as follows:—

"1. A fluid modification of Mueller and Miller's medium for selective cultivation of Corynebacterium diphtheriae is described. By employment of Moncton's principles of cultivation (i.e. short enrichment in the new fluid medium before transferring onto solid media) it was possible to obtain positive cultivation of small inocula of Corynebacterium diphtheriae also when the swab was artificially contaminated by organisms of throat origin (Micrococcus pyogenes, M. epidermidis,

Streptoc. salivarius, E. coli) in up to 400,000 fold amounts. The growth of Streptococcus faecalis is inhibited in a small degree or not at all; if present abundantly the growth of Corynebacterium diphtheriae from large inocula may be suppressed.

"2. The steps of examination are as follows: Swabs after being smeared on blood agar plates (for streptococci and staphylococci) are immersed in the new medium. After 6 hours' (in urgency) and/or 24 hours' (in urgency and in search for carriers) incubation the swab is rubbed on blood agar plate, spread with platinum loop, and the plates are further incubated. The identification of Corynebacterium diphtheriae, including toxicity tests in guinea pig, may be complete in 48 hours.

"3. In routine tests the positive cultivation of Corynebacterium diphtheriae with the new medium was superior by 15–40 per cent than when solid selective media was employed (i.e. Clauberg's medium). In the latter great variability was noted in promotion of growth from small inocula."

RAYNAUD, M., ALOUF, J. & MANGALO, R. Croissance et toxinogénèse diphtériques en culture agitée, sur milieu synthétique. [**Diphtheria Bacillus growth and Toxinogenesis in Agitated Cultures, on Synthetic Media**] *Ann. Inst. Pasteur.* 1959, Mar., v. 96, No. 3, 276–88, 2 text figs. & 2 figs. on pl. [31 refs.]

An explanation was sought of the divergence between earlier results of the French workers and those of YONEDA and PAPPENHEIMER [this *Bulletin*, 1958, v. 33, 509]. The latter maintain that growing the strain Yoneda in a medium of defined composition they only got traces of toxin secretion in the earlier phases of growth and that toxin was mainly liberated later on death of the bacteria.

The authors, however, had observed free secretion of toxin both in complex and in partly defined media during the period of exponential growth.

They selected actively toxigenic colonies from the Yoneda strain and grew them in defined medium of which full details are given. This was modelled on that of Yoneda.

Study of toxin production was by intradermal titration in the rabbit, by flocculation according to RAMON and by the tube gel diffusion method of OAKLEY and FULTHORPE [*ibid.*, 1953, v. 28, 656] and the plate diffusion modification of OUCHTERLONY.

The *in vivo* titration and the Oakley and Fulthorpe method both revealed active secretion of toxin in the earliest stages of experimental growth when it was not revealed by the less delicate tube flocculation and plate gel diffusion tests. *J. W. McLeod*

RAYNAUD, M., RELYVELD, E. H., GIRARD, O. & CORVAZIER, R., with the technical collaboration of O. BEPOLDIN & F. AUTIN. Préparation de sérums antidiphtériques de titre floculant élevé et de faible pouvoir neutralisant par immunisation de chevaux sans immunité de base (Schick positifs) avec une anatoxine de haute pureté. [**Preparation of Anti-Diphtheria Sera of High Flocculating Titre and Low Neutralizing Capacity, by means of Immunization of Schick-Positive Horses with a Highly Purified Toxoid**] *Ann. Inst. Pasteur.* 1959, Feb., v. 96, No. 2, 129–39, 2 figs. & 2 pls. [50 refs.]

The difficulty of getting antisera of good neutralizing titre for diphtheria toxin from horses with low content of plasma antitoxin at the outset has been emphasized in the past. When, however, immunization is started with toxoid of high purity, good flocculating sera are obtained which at the first have relatively low neutralization power. If the immunization is continued, however, the neutralizing titre rises and approaches a ratio of 1 to the flocculating antibody. This happens even though crude toxoid is used for later injections. The samples of serum withdrawn late in the course of immunization show replacement of gamma by $beta_2$ globulin and give multiple lines of precipitation when diffusing in gel against toxin. *J. W. McLeod*

JENSEN, K. A. **Laboratory Techniques applicable in the Tropics.** *Acta Tuberculosea Scandinavica.* 1959, Suppl. 47, 182–93, 4 figs.

The author stresses that there is no fundamental difference between the techniques used in temperate zones and those used in the tropics, but the methods used depend on the laboratory conditions and the trained personnel available. The 2 methods described in detail in the appendix are direct microscopical examination and cultivation after treatment with 4% sodium hydroxide on a modified Petragnani medium with and without isoniazid, PAS and streptomycin.

The value of the simple direct examination is illustrated by the finding that of 1952 specimens of sputum examined during 1940–2, 87 were positive by direct microscopy. Also, treatment with the antituberculous drugs can be considered to be satisfactory when the number of bacilli in the direct smear shows a steady decrease; conversely an increase in the number is indicative of drug-resistance.

Cultivation of the specimen, necessitating only an incubator as the additional apparatus, was made in the medium supplied from the Central Laboratory. This medium was also available in a form containing a mixture of the drugs and it remained satisfactory for at least 6 months when stored at 4°C. The concentrations of the drugs used were 8 μgm. streptomycin, 0·8 μgm. PAS and 0·16 μgm. isoniazid per ml.

The classification of the strains based on the catalase and niacin tests, along with the sensitivity tests, is recommended as these tests do not necessitate additional expensive apparatus. *S. R. M. Bushby*

RUNYON, E. H., SELIN, M. J. & HARRIS, H. W. **Distinguishing Mycobacteria by the Niacin Test. A Modified Procedure.** *Amer. Rev. Tuberculosis.* 1959, May, v. 79, No. 5, 663–5.

Of the mycobacteria, only human tubercle bacilli are known to produce significant quantities of niacin. KONNO [this BULLETIN, 1957, v. 32, 799] described a test that could be used routinely for this purpose but occasional false-negative results are obtained. In the

present report a technique is described which is claimed to be more reliable and to be suitable for either fluid or solid cultures.

In the case of a solid culture, 0·5–1·0 ml. of water is added and layered over the growth. After 5 minutes, during which the niacin will have been extracted, 0·25–0·5 ml. of the water is removed and if there are bacilli present or if a fluid culture is used, they are removed by centrifuging. To the extract or culture fluid, equal volumes of 4% alcoholic aniline and 10% aqueous cyanogen bromide are added. (A fume hood must be used for this latter step.) When niacin is present a yellow colour develops immediately. (Addition of an alkaline germicide will stop the further development of the tear gas.)

An alternative method which avoids the tear gas but gives a less intense colour is the use of 5% chloramine T for the aniline and 1% sodium or potassium cyanide for the cyanogen bromide.

The colour produced from human tubercle bacilli is faint only when the growth is sparse but the extraction period can then be extended to 30 minutes. A control consisting of an extract from the medium should always be included in the test.

This method was tested on strains grown on 5 media and only the pink colour from blood media interfered with the results. In a comparison made on 41 strains by Konno's method and this modification, 18 strains gave doubtful or negative results with the former method but all were positive by the new method, and of 76 other mycobacteria tested, a strong positive reaction was produced only by the vole bacillus and a weak positive by *Mycobacterium ulcerans*.

The modified test can be used on pigmented strains and malachite green in the medium does not interfere with the reading. The increased sensitivity seems to be due to the extraction of the niacin from the medium. *S. R. M. Bushby*

COPLEY, A. L., MAUPIN, B. & BALÉA, T. **The Agglutinant and Adhesive Behaviour of Isolated Human and Rabbit Platelets in Contact with Various Strains of Mycobacteria.** *Acta Tuberculosea Scandinavica.* 1959, v. 37, Nos. 1/2, 151/61, 4 figs. [19 refs.]

From the observation that tubercle bacilli injected intravenously into hamsters, guineapigs or rabbits can be seen adhering to agglutinated platelets in the capillaries, the suggestion has been made that the primary reaction after the invasion of these bacilli into the bloodstream is their removal by adhering to the platelet agglutination thrombi produced [see, for example, this *Bulletin*, 1955, v. 30, 1058, 1059].

In the present paper *in vitro* experiments are described in which this clumping of the bacilli and the platelets, suspended in plasma, is shown to be increased when the plasma is from man or rabbit immunized with BCG. The factor responsible for this mutual clumping is apparently absent from serum and it is not destroved by heating at 55°C., for 30 minutes.

The authors intend to investigate further the phenomenon, which they term "bacillo-platelet conglutination" thus expressing the simultaneous adhesion of the platelet and the bacilli, and they suggest that this increase in adhesiveness is of fundamental importance in immunological reactions. *S. R. M. Bushby*

RHEINS, M. S. & BUEHLER, E. V. **Antigenicity of Antimycobacterial Serums.** *Amer. Rev. Tuberculosis.* 1959, May, v. 79, No. 5, 631–40, 6 figs. [11 refs.]

SEIBERT *et al.* (*Amer. Rev. Tuberculosis*, 1956, v. 73, 547; *J. Infect. Dis.*, 1956, v. 99, 76) have made the suggestion that serum polysaccharides interfere with the detection of antibodies in tuberculous sera and the results of the experiments described in the previous paper by the present authors [see above] indicated a method that could be used for demonstrating such interfering polysaccharides.

Rabbits were injected with serum taken at intervals from other rabbits during immunization with viable tubercle bacilli (including BCG) and at intervals these second rabbits were bled and their sera tested with tuberculin-sensitized sheep red cells and with trypsinized human red cells.

The results show that whereas in the rabbits injected with the adjuvant alone or with normal serum antibodies of low titre for both types of cells were detected and these were mutually cross-adsorbable, injection of the tuberculous antisera produced agglutinins which were detectable only by the tuberculin-sensitized cells and which were present in titres some 4 times higher (1 : 16) than the antibodies for the trypsinized cells.

The highest titre of the tuberculous antibodies was produced by sera taken from the infected rabbits 5–7 weeks after injection, at the time when the agglutinins of these original rabbits were declining. Adsorption of the tuberculous antisera with the sensitized cells before injection into the rabbits did not reduce the antibody response but in some instances actually enhanced it.

Serum from rabbits immunized with either dead or saprophytic mycobacteria produced only antibodies that were similar to those produced by normal sera.

The authors concluded from these experiments and of those of the previous paper, that at least 2 antigenic components are adsorbed by sheep cells from Old Tuberculin; one of these apparently possesses a specificity identical with that of trypsinized human red cells, and the other component, assumed to be a tuberculopolysaccharide, detects not only the antibodies present in antituberculous sera but also those produced by the serum of animals infected with tubercle bacilli. The antigen present in these tuberculous sera is therefore probably a polysaccharide, possibly derived from the animals' tissues. *S. R. M. Bushby*

BÖNICKE, R. & LISBOA, B. P. Über das Vorkommen von Acylamidasen in Mycobakterien. I. Mitteilung. Die enzymatische Desamidierung aromatischer und aliphatischer Carbonsäureamide. [**On Acylamidases in Mycobacteria. I. Communication: The Enzymatic Desamidation of Aromatic and Alipathic Carbonylamids**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 5/6, 403–21, 12 figs. [16 refs.]

GASTAMBIDE-ODIER, Mireille. **Determination of Dehydrogenases in Atypical Strains and in Other Mycobacteria.** *J. Bacteriology.* 1959, June, v. 77, No. 6, 748–52. [31 refs.]

MANKIEWICZ, E., STACKIEWICZ, E. & LIIVAK, M. **A Polysaccharide isolated from *Candida albicans* as a Growth-Promoting Factor for *Mycobacterium tuberculosis*.** *Canadian J. Microbiol.* Ottawa. 1959, June, v. 5, No. 3, 261–7, 2 figs. [13 refs.]

In previous papers the cells and extracts of *Candida albicans* were reported to accelerate the growth of tubercle bacilli [this *Bulletin*, 1955, v. 30, 633; *ibid.*, 1957, v. 32, 991] and the authors now claim to have isolated from this fungus a polysaccharide which has a very definite effect on the growth of tubercle bacilli.

The polysaccharide was isolated by rupturing the cells with glass beads, precipitating the proteins by either heat or the addition of ammonium sulphate and then extracting with chloroform. After dialysis 3 parts of ethanol were added to the extracted fluid and the precipitate which formed was collected, dissolved in water and re-precipitated with ethanol.

The precipitate which represented 10% of the dry-weight of the cells contained less than 2% nitrogen and watery solutions contained only traces of reducing sugars. Acid hydrolysates were ninhydrin-negative, but contained reducing sugars, and paper chromatography revealed the presence of glucose and mannose.

Added to complete media, *e.g.* Dubos, Kirchner or Löwenstein medium, at a concentration equivalent to 10 mgm. of the dried cells per ml., the polysaccharide promoted the growth of inocula of H37Rv and BCG, 100 times smaller than those capable of growing on the unsupplemented media. Added to an incomplete medium, consisting of salts, glycerol and asparagine, the same concentration of the extract permitted the growth of these 2 strains of tubercle bacilli although to a lesser extent than did the Dubos medium.

The polysaccharide was capable of replacing streptomycin for a streptomycin-dependent strain of tubercle bacilli, perhaps because of the similarity between it and the streptose of streptomycin. When 20 mgm. were added to Löwenstein medium on which 322 pathological specimens from patients undergoing treatment with isoniazid or streptomycin or both were cultured, 92 were positive for tubercle bacilli and of these only 21 grew on the medium without the polysaccharide.

S. R. M. Bushby

COSTELLO, R. L. & HEDGECOCK, L. W. **Effect of Metavanadate Ion on the Growth *in vitro* of *Mycobacterium tuberculosis*.** *J. Bacteriology.* 1959, June, v. 77, No. 6, 794–9, 1 fig. [18 refs.]

"The effect of vanadium ion on the growth *in vitro* of *Mycobacterium tuberculosis* in a defined medium was studied. The stimulation of growth by this metal reported by other investigators was not confirmed. Instead, the metal was found to be inhibitory to the growth of this organism. This inhibition was most marked in the presence of polyoxyethylene sorbitol monooleate (Tween 80). The inhibitory effect of vanadium varied with different saprophytic species of mycobacteria.

"A similar inhibitory action was found with manganous ion and chromate ion. The inhibition caused by vanadium was reversed, however, by minute quantities of either. A possible competitive relationship was apparent. Titanium and iron were not appreciably inhibitory to the growth of *M. tuberculosis*. However, both titanium and ferrous (but not ferric) iron appeared to produce an additive inhibitory effect with vanadium.

"The inhibitory action of vanadium was diminished in the absence of Tween 80 or in the presence of bovine albumin. There was no quantitative relation between the amount of Tween 80 present and the concentration of vanadium required to inhibit growth. Bovine albumin apparently decreased the inhibitory activity by binding the metal."

FONG, J., CHIN, D., AKIYAMA, H. J. & ELBERG, S. S. **Studies on Tubercle Bacillus-Monocyte Relationship. III. Conditions affecting the Action of Serum and Cells. Modification of Bacilli in an Immune System.** *J. Exper. Med.* 1959, June 1, v. 109, No. 6, 523–43. [17 refs.]

In previous publications [see this *Bulletin*, 1957, v. 32, 618 *bis*, 1958, v. 33, 195] the authors showed that the sera of animals immunized with various antigens, *i.e.* BCG, *Salmonella, Brucella*, and ovalbumin, protect monocytes from rabbits immunized with BCG or *Brucella* against the necrotizing action of virulent tubercle bacilli, but not those from non-immune rabbits or from rabbits immunized with *Salmonella*. These observations are extended in the present paper.

Absorption of the protecting immune sera with the homologous antigens is shown not to alter the degree of protection, and immune globulin from pooled anti-BCG sera affords less protection than whole immune serum. Heating the serum at 60–70°C. failed to destroy the protective factor, and dialysing did not remove it.

In other experiments in which monocytes and sera were collected 5 days after immunization with living and dead BCG, the protective action of the serum was shown to be present by this time and thus not to be related to the state of tuberculin sensitivity; the immunity of the cells had not developed by this stage with the dead antigen although it had with the living BCG.

Exposing H37Rv for 15 hours to immune serum was shown not to affect their necrotizing action on immune monocytes suspended in non-immune serum, and neither was the cultivation of the immune monocytes in immune serum effective in preventing the action of the virulent tubercle bacilli in non-immune serum; for the immune serum to exert its protective action continuous contact after phagocytosis was shown to be essential. Phagocytosed tubercle bacilli, from immune monocytes that had been protected by immune serum, however, and transferred to non-immune monocytes in the immune serum, showed a decreased necrotizing action; the nature of this change was not studied but

the authors suggest that it is due to a change in the surface of the bacilli rendering them more sensitive to the combined action of the immune serum and the enzyme systems of immune monocytes.

S. R. M. Bushby

HENNES, A. R., MUCHMORE, H. G., MCCLURE, H. G. & HAMMARSTEN, J. F. *In vitro* **Inhibition of Growth of *M. tuberculosis* by certain 11-Oxygenated Steroids.** *Proc. Soc. Exper. Biol. & Med.* 1959, May, v. 101, No. 1, 145–7, 1 fig. [11 refs.]

Hydrocortisone and corticosterine in concentrations of 100 μgm. per ml. markedly inhibited the growth of isoniazid-sensitive and resistant strains of tubercle bacilli in a synthetic medium containing Tween 80.

This concentration of the steroids is well above those in the blood after intravenous injection but as the drugs may become concentrated in the tissues, the concentration of the corticosteroid may be sufficient to counteract its depressing effects on the host's reaction to the infection; undoubtedly the concentrations after intrathecal injection may equal or exceed the *in vitro* inhibiting concentration.

The authors suggest that a bacterial system of this type might be of use both for determining the nutritional requirements of the tubercle bacillus and for studying *in vitro* the effects of certain mammalian steroid hormones. *S. R. M. Bushby*

ARAKAWA, T., OOTA, M. & SATO, Y. **Approximate Estimation of Tuberculin-Polysaccharide in Serum. (Studies on Tuberculosis in Infancy and Childhood. 4th Report.)** *Tohoku J. Exper. Med.* 1959, Feb. 25, v. 69, Nos. 2/3, 295–301.

In a previous paper (*Tohoku J. Exper. Med.*, 1958, v. 68, 99) the authors showed that when tuberculo-polysaccharide was added to blood containing specific antibodies sensitization of the red cells did not occur until the antibody was completely neutralized; they therefore suggested that the detection of sensitized red cells in tuberculous patients is of diagnostic and prognostic value. In the present paper they describe a method for estimating the quantity of combined tuberculo-polysaccharide in patients in whom the antibody is in excess.

The method consists of heating the serum at 100°C. after the addition of *p*H 3·0 buffer. The mixture is filtered, the filtrate adjusted to *p*H 7·0 and 2-fold serial dilutions made. To the series of dilutions is then added a volume of standard antituberculous serum and after 3 hours at 37°C. tuberculin-sensitized cells are added. The concentration of the tuberculo-polysaccharide is deduced from the extent of inhibited agglutination.

[The paper includes the results of a control experiment in which varying quantities of tuberculo-polysaccharide were added to a constant volume of diluted immune serum, the antibody content of which was known to be in excess of the maximum concentration of the added antigen. The recovery of the antigen was, however, shown to vary with the concentration *e.g.* it was 1 : 16, 1 : 4 and 1 : 2 with concentrations of 118, 237 and 950–1,900 μgm.%, and therefore a standard titration is essential. The authors have apparently not investigated the effects of variations in the antibody content.] *S. R. M. Bushby*

KURYLOWICZ, W., KUZNIECOW, A., PASQUIER, J. F. & SITEK, K. **The Comparative Study of Lyophilized BCG Vaccines prepared from BCG Strains of Different Origin.** I. *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 10, 1649–57, 6 figs. [Translated from Russian.]

This investigation was undertaken in an attempt to find differences between strains of BCG that could account for the variable effects that follow vaccination with this organism; the 5 strains examined were of Danish, French, Brazilian, Swedish and Soviet origins.

The strains, having been grown in Sauton medium, harvested, washed, dried in a bacterial press, and triturated in a rotary shaker with steel balls for 6 minutes, were freeze-dried, the desiccating medium being 10% sucrose and 1% gelatin. Each ampoule contained 1 mgm. of dried bacilli and reconstitution of the vaccine occurred in 30 seconds.

Determination of the number of viable units present in the ampoules before and after drying was made by Krohn's method, with Löwenstein-Jensen medium, and by the slide-culture method of Price in Youmans medium; the Krohn method gave counts almost 4 times higher than those of the slide methods [the original Russian version is confused on this point, but this is the general finding; the statement in line 2, p. 1655 of the English version is the reverse of the Russian]. The largest number of viable units was found with the Brazilian strain but the recovery after drying was only about 50% with all the strains.

In Youmans medium without a surface-active agent the Danish, French and Soviet strains produced cording; none of the strains produced progressive lesions in guineapigs.

Differences were observed between the rates that the Danish, French and Brazilian strains developed resistance to isoniazid and streptomycin during serial passage; the Danish strain was the first to become resistant to isoniazid whereas the French strain was the first to become resistant to streptomycin.

S. R. M. Bushby

KURYLOWICZ, W., KUZNIECOW, A., PASQUIER, J. F. & SITEK, K. **Attempts to Differentiate BCG Strains of Different Origin and Lyophilized Vaccines prepared from these Strains by means of Radioactive Carbon, ^{14}C.** II. *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 11, 1759–69, 10 figs. [14 refs.] [Translated from Russian.]

Tubercle bacilli growing in Dubos medium with no glucose but to which had been added 10 μC per ml. sodium acetate containing ^{14}C in the methyl group, become radio-active, the activity in the bacilli per unit volume of the culture increasing from the 7th to the 9th day and then falling sharply. The curve of this fall varies in shape, depending on the strain of bacilli and the type of inoculum. Dubos cultures and lyophilized vaccines of 5 strains of BCG of Danish,

French, Swedish, Soviet and Brazilian origins, were examined by this method, but only the Brazilian one was shown to differ; it differed in the rapidity with which the ^{14}C was absorbed and in showing 2 peaks of absorption.

When radio-active bacilli of this Brazilian strain were injected intravenously into mice, viable counts showed that the bacilli initially multiplied rapidly in the spleen but they decreased from the 2nd week onwards; the radio-activity was, however, lost more rapidly, indicating an exchange *in vivo* of ^{12}C for ^{14}C. When the rates of loss of radio-activity from the spleen, lungs and liver were compared with those from these organs of mice inoculated with radio-active H37Rv, no differences were observed. Per unit weight of tissue, however, the lungs appropriated the radio-activity with the BCG at twice the rate of the spleen and almost 14 times that of the liver, while with H37Rv the appropriation by the lungs was 4 times as great as that by the spleen, and 30 times that by the liver.

The immunizing properties of the lyophilized vaccines of the 5 strains were also compared in mice. The mice were challenged 30 days after vaccination with radio-active tubercle bacilli of the Vallée bovine strain and 48 hours later the radio-activity of the tissues was compared with that of unvaccinated animals. From the results the Danish strain was considered the most immunogenic vaccine and the Brazilian the least active.

The strains were also assessed in infants, and statistical analysis of the results indicated that the Brazilian strain gave rise to allergy to a lesser extent than either the French or Danish strains, although the difference was not of practical importance; this vaccine also caused a lower incidence of lymphatic reactions.

In addition to these differences, the Brazilian strain was shown to exhibit no cording, to contain more viable bacilli per mgm. of lyophilized vaccine, and to acquire resistance to streptomycin and isoniazid at a different rate and degree from the other strains.

On the basis of these results the Brazilian vaccine was introduced into the Polish People's Republic from January 1955. *S. R. M. Bushby*

Kötsche, W. & Kunz, H. H. Versuche zur Virulenzsteigerung des BCG im Sinne einer aktiven Tuberkulose durch Passagen in virusdurchseuchten Meerschweinchen. [**Attempts to Increase the Virulence of BCG towards the Production of Active Tuberculosis in Guineapigs infected with Viruses**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 1/2, 101–17, 5 figs. (1 coloured on pl.) [15 refs.]

BCG was carried through 5 passages in a total of 1,204 guineapigs by intraperitoneal inoculation alternating with subculture on nutrient medium. Most of the animals had been previously infected with foot-and-mouth disease, MM or lymphocytic choriomeningitis viruses and had subsequently recovered. The animals were killed 3–4 months after infection with BCG and subjected to autopsy, and the morbid anatomical and bacteriological findings are described in detail. No evidence of any increase in the virulence of the strain as a result of passage was obtained.

D. J. Bauer

Desbordes, J. Rapport sur la tuberculine. Projet de contrôle international de la tuberculine. [**Report on Tuberculin. Project for the International Control of Tuberculin**] *Arch. Belges Méd. Sociale, Hyg., Méd. du Travail et Méd Légale.* 1959, Mar., v. 17, No. 3, 153–99.

This is a report presented to the 4th International Congress of Biological Standardization, Brussels, July 1958. In the Introduction the nature of tuberculin is discussed and, in the absence of a chemical method of estimation, the need for biological standardization is emphasized.

In Parts I, II and III the replies to certain questionnaires are given and summarized in tables. The questionnaires, which were sent to authorities in 23 countries, were concerned with the methods used by these authorities for the preparation of tuberculin. They dealt with the precipitation, purification, standardization, sterility testing, and the nature of the antiseptics used. The diversities of many methods in use is clearly evident from the replies.

In the fourth and final Part the author presents definite recommendations for standardization of the various stages in the preparation of this reagent, and which he hoped would form the basis for discussion.

[The original of this review should be read by those actively interested in this subject.]

S. R. M. Bushby

Buehler, E. V. & Rheins, M. S. **Serologic Relationship of Old Tuberculin-Sensitized Sheep Erythocytes and Trypsinized Human Erythrocytes.** *Amer. Rev. Tuberculosis.* 1959, v. 79, No. 5, 622–30. [32 refs.]

Rabbits injected intravenously with sheep and rabbit red cells sensitized with OT produced antibodies to the adsorbed antigens, and although similar antibodies were produced by the injection of OT diluted 1 : 15, the response was apparently enhanced by the antigens being present on the cells, for the rabbits injected with the sensitized cells gave the higher titres. The response also appeared to be affected by the carrier cell, for not only were higher titres obtained with the sheep cells but with these cells the maximum titres with a subsequent fall occurred on the 5th day whereas it was on the 12th day with the rabbit cells. Also, haemolysins were detected with the sensitized sheep cells but not with the sensitized rabbit cells; the rabbit cells, however, readily adsorbed the haemolytic antibodies.

Human red cells treated with trypsin for 10 minutes were shown to agglutinate to low titres (1 : 4) in rabbit sera, and although these titres could not be increased by immunization with various mycobacterial antigens, the antibodies were adsorbable by sheep cells sensitized with OT although several adsorptions were usually necessary to do this; trypsinized human cells would not, however, remove tuberculous antibodies.

Antibodies to trypsinized human cells and to sheep cells sensitized with OT were also demonstrated in

rabbits immunized with various non-mycobacterial antigens, which included viruses and sera of other animals, and although adsorption with the sensitized cells invariably removed the antibodies from the trypsinized human cells adsorption with the human cells did not always remove those for the sensitized sheep cells.

These results are interpreted as indicating that adsorption of the antigens in OT antigen and trypsinization so modifies the red cells that they then possess a common antigen. This effect is reminiscent of that of the Thomsen-Friedenreich phenomenon in which a "T" antigen of red cells is revealed by the enzymatic action of certain bacteria. *S. R. M. Bushby*

WASSERMAN, J. & PACKALÉN, T. **The *in vitro* Effect of Specific and Nonspecific Bacterial Products on the Migration of Leukocytes from Tuberculin-Sensitized Guinea Pigs.** *Amer. Rev. Respiratory Dis.* 1959, July, v. 80, No. 1, Pt. 1, 19–25, 1 fig. [22 refs.]

"Old Tuberculin and certain nonspecific bacterial products were tested for their inhibitory action *in vitro* upon the migration of leukocytes from tuberculin-sensitized guinea pigs. Cytotoxicity was displayed by Old Tuberculin, as well as by filtrates of *E. coli* cultures and lipopolysaccharides of *E. coli* and *Serr. marcescens*, but not by pneumococcal polysaccharide."

FREUND, J. & STONE, S. H., with the technical assistance of J. H. GOODE. **The Effectiveness of Tuberculo-Glycolipid as an Adjuvant in eliciting Allergin Encephalomyelitis and Aspermatogenesis.** *J. Immunology.* 1959, June, v. 82, No. 6, 560–67, 1 fig. [18 refs.]

ROBSON, J. M. & SULLIVAN, F. M. **The Effect of Treatment with a Large Dose of Isoniazid on an Established Tuberculous Infection in Mice.** *Brit. J. Pharmacol. & Chemotherapy.* 1959, June, v. 14, No. 2, 222–8, 1 fig. [16 refs.]

In these experiments mice were inoculated intracorneally with bovine tubercle bacilli. When the inoculation is by this route there is both rapid multiplication of the bacilli and cellular invasion, the lesion becoming visible within 10 days. Although there is little multiplication of the organisms after the second week the lesion continues to increase in size until much of the cornea becomes involved. Although after reaching a maximum size the lesion remains constant for many months, there is a progressive systemic spread of the disease. Immunity, shown by the failure of a similar inoculation into the other cornea to produce a lesion, can be detected within a week and shown to persist for at least 13 months [this *Bulletin*, 1959, v. 34, 162].

In these experiments treatment with 3·0 mgm. isoniazid per day in the diet was started on the 14th day of infection and continued for as long as 11 months in some of the animals. This treatment arrested the spread of the corneal lesion and although there was some decrease in size, the lesion became stabilized at about one-third the size of that of the untreated mice. The reduced size was accounted for partly through effects on the main core of the lesion but also by the disappearance of perifocal inflammation. The treatment did not, however, eliminate the acid-fast bacilli for they were still present after many months of treatment although few of them or of those of the untreated animals could be grown in culture. The persistence of the perifocal inflammation in the untreated animals, in spite of the bacilli being apparently non-viable, suggests either that the bacilli were still capable of a biochemical effect on the tissues, or alternatively that the isoniazid suppressed the tissue response.

The treatment also prevented the systemic spread of the disease, presumably by inhibiting the multiplication of the bacilli after they had been carried to other tissues. This effect is of especial interest, for it occurred in spite of the treatment shortening the duration of the immunity; in these treated animals there was little evidence of immunity after 5 months, presumably owing to the reduction in the antigenic stimulus.

S. R. M. Bushby

KUBALA, E.; URBANCÍK, R. **The Isoniazid Resistant Strains of *M. tuberculosis*: I. The Behaviour *in vitro* and Resistance Determination** [KUBALA & URBANCIK]. *Giorn. Ital. di Chemioterap.* Milan. 1958, Jan.–Dec., v. 5, Nos. 1/4, 85–94. [54 refs.] **II. Pathogenesis and Chemotherapy of Experimental Tuberculosis caused by INH Resistant Strains** [URBANCIK & KUBALA]. *Ibid.*, 95–106. [61 refs.]

These 2 articles come from Czechoslovakia and are essentially reviews of the subject, especially of work of American and British investigators. The first deals with the problem of defining isoniazid-resistance, the mode of action of the drug, the difficulties in growing the resistant variants, and some of the causes of failure of chemotherapy. They refer to some of their own experiments in which they demonstrated that para-aminobenzoic acid (PAB) enhanced the activity of isoniazid for resistant strains in fluid media although not in solid media, an effect not seen with streptomycin. They conclude that little is known about the precise mode of action of isoniazid and the cause of increased resistance.

In the second article the differences in the behaviour of isoniazid-sensitive and -resistant strains in animals is discussed in relation to the known enzymatic differences between the strains. The different factors involved in the defence of the body against tuberculosis and the possible differences between the sensitivity of guineapigs and mice to the isoniazid-resistant strains are also discussed. As for the clinical use of the drug, the authors emphasize that there are two aspects that need especial consideration. Firstly, whether treatment should be continued after resistant organisms have been detected, especially as there is the possibility that these strains are avirulent; to the authors, however, the deliberate aim of producing resistance seems most unwise. Secondly, what form of therapy should be used to lessen the incidence of resistance and here, although the authors accept the value of combined therapy, they

suggest that other methods should be tried such as those which might increase the sensitivity of the resistant variants, *e.g.* the simultaneous administration of PAB. *S. R. M. Bushby*

DUNBAR, F. P., MCALISTER, Elizabeth & JEFFERIES, Mildred B. **Catalase and Peroxidase Activities of Isoniazid-Susceptible and -Resistant Strains of *M. Tuberculosis*. Relationship Between the Results of a Test for Enzymes and those of the indirect Drug-Susceptibility Test.** *Amer. Rev. Tuberculosis.* 1959, May, v. 79, No. 5, 669–71.

This report describes the results of examining 1,221 cultures of tubercle bacilli isolated from hospital patients for isoniazid sensitivity and catalase and peroxidase activities.

The sensitivity tests were done on Löwenstein-Jensen medium and the enzymatic activities detected by flooding the control slope of the tests, containing no drug, with 0·5% hydrogen peroxide and 0·1% catechol. The colonies that produced bubbles within 2–5 minutes were regarded as positive for catalase and those that turned brown to black within 45 minutes as positive for peroxidase.

Of the 869 catalase-positive cultures, 55·6% were susceptible to isoniazid (1·0 μgm./ml.), 20·4% were partially resistant and 24% were resistant (maximum growth in the presence of 1 μgm./ml.), while of the 552 peroxidase-positive cultures, only 10·7% were partially resistant and 8·9% were fully resistant. Of the 542 cultures that were catalase and peroxidase positive, 81% were isoniazid susceptible. Of the 80 cultures which contained both catalase-positive and -negative colonies, the majority were also peroxidase deficient and 70 of them contained isoniazid-resistant colonies. Of 265 cultures negative for both enzymes, only 7 were composed entirely of isoniazid-susceptible organisms.

Catalase activity was exhibited by the vast majority of cultures that showed peroxidase activity but peroxidase activity was not shown by a large number of colonies that were catalase positive, and when these differences were correlated with isoniazid sensitivity, the presence of peroxidase was found to be more significant than that of catalase with sensitive strains, but negative catalase or negative peroxidase was presumptive evidence of isoniazid resistance. *S. R. M. Bushby*

JENEY, E. & ZSOLNAI, T. Versuche zur Entdeckung neuer Tuberkulostatika. V. N-Aryl-Derivate der o-Dicarbonsäure-imide. [**Search for New Tuberculostatics. V. N-Aryl Derivatives of O-Dicarbonic Acid Imides**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 1/2, 118–23.

The N-4-ethoxy-phenyl and N-4-chloro-phenyl derivatives of malic imide, succinic imide, phthalic imide and 2,5-dimethyl-pyrrol (*i.e.* 8 compounds in all) were tested for tuberculostatic activity *in vitro*: 5 showed moderate activity and 3 none. In therapeutic tests in guineapigs inoculated with tubercle bacilli no significant effect was produced by any of the compounds.

L. P. Garrod

ROSS, M. R., MONKIEWICZ, J. & BOWMAN, E. K. **Bacteriophage Typing of *Staphylococcus aureus* in Plastic Trays.** *Pub. Health Lab.* 1959, Mar., v. 17, No. 2, 29–32.

A method of bacteriophage typing of staphylococci is described. Transparent plastic trays are used containing 8 rows of 12 holes of 2 ml. capacity. Sterile medium is dispensed into each hole with a pipette syringe and trays are irradiated with ultra-violet light and wrapped in aluminium foil for storage.

8 strains can be typed in 2 trays. The drop of broth culture is put on to each horizontal row of 24 holes and rotated to distribute; the 24 phages are added to the vertical rows by pipettes fitted with needles. Trays are re-covered with foil and incubated.

Trays are disinfected by immersion overnight in disinfectant and they are rinsed in tap water. They are re-immersed in the solution overnight, rinsed and dried before re-use.

Results of typing 10 cultures by this method and by the conventional method were identical.

[This method is economical in agar but one wonders if this advantage is not outweighed by the additional time taken to prepare the trays and inoculate the holes when large numbers of strains are involved.]

M. Patricia Jevons

TOMIC-KAROVIC, K. & SKALOVA, R. S. **Prevalence of the Bacteriophage Types of Staphylococci in Various Sources.** *Bull. Sci. Yougoslavie.* 1959, Apr., v. 4, No. 4, 111–12.

ROUNTREE, Phyllis M. **Changes in the Phage-Typing Patterns of Staphylococci following Lysogenization.** *J. General Microbiol.* 1959, June, v. 20, No. 3, 620–33. [15 refs.]

In the course of investigations of the possible origin of staphylococci of the epidemic type 80/81 phages were isolated that were able to confer immunity to the phages 80 or 81, but which were different from these phages. 2 strains of phage type 52/52A/80/81 were found to be lysogenic for phages which could convert strains of type 80/81 to the pattern 52/52A/80/81; they also ceased to show an "inhibitory reaction" with phage 47C. 5 such converting phages were studied in detail. Lysogenization of strains of type 80/81 by the converting phages usually gave rise to cultures having the same phage type as the staphylococcus from which the converting phage was derived. It should be noted that strains of type 80/81 generally show "inhibition" by strong filtrates of phages; Rountree considers this inhibition due to absorption of the phage leading to death of the cell without multiplication of the phage.

The conversion of typing patterns from 80/81 to 52/52A/80/81 could not be explained on the basis of prophage substitution nor on the basis of some alteration in the ability of the cells to absorb phages 52 and 52A. Some evidence was, however, obtained that a small number of mutants with the pattern 52/52A/80/81 were already present in 80/81 strains, perhaps especially in 18 hour cultures. It is suggested that the treatment of the 80/81 culture with the converting

phage selects the mutants because they are more readily lysogenized and thus protected from lysis.

A few examples are recorded in which conversion of staphylococci from type 80/81 to 52/52A/80/81 seems to have occurred *in vivo*.

It is postulated that the basic pattern of phage sensitivity of this set of strains was 47C/52/52A/80/81 and that various patterns have been derived from this by combinations of mutation and lysogenization.

[See also ASHESHOV & RIPPON, below.]

R. E. O. Williams

ASHESHOV, Elizabeth H. & RIPPON, Joan E. **Changes in Typing Pattern of Phage-Type 80 Staphylococci.** *J. General Microbiol.* 1959, June, v. 20, No. 3, 634–43. [17 refs.]

It was noted that in epidemics due to staphylococci of phage type 80, strains of type 52/52A/80 were also isolated. In experiments to determine whether the latter could arise from the former, it was found that some 52/52A/80 strains did in fact carry phages which, when they lysogenized type 80 strains, converted them to the 52/52A/80 pattern. 3 different varieties of phage were observed and the phage pattern of converted strains usually corresponded to the strain from which the converting phage was derived. The converting phages were very similar to those isolated by ROUNTREE [above]. They could be distinguished by the resistance patterns they conferred against one another when used separately to lysogenize a single strain of type 80.

4 hypotheses were considered to explain the conversion of type 80 strains to 52/52A/80. In the ordinary way lysogenization leads to phage immunity rather than to a gain in sensitivity. Lysogenic conversion, on the lines of the conversion of non-toxigenic to toxigenic *Corynebacterium diphtheriae* was excluded when it was found that continued presence of the converting phage was not needed. Transduction was not tenable because the effect was too efficient and was not dependent on the character of the cell on which the phage was last propagated. ROUNTREE's hypothesis of selection of pre-existent mutants was examined but rejected because no such mutants could be found, and because the frequency of lysogenization of a converted strain that had been "delysogenized" did not differ from that of its original unconverted parent. Prophage substitution could not be supported because no phages could be detected in the type-80 strains, though it is possible that these strains produce only "defective" phages. Thus no satisfactory explanation is apparent.

R. E. O. Williams

GRIFFITH, L. J. & OSTRANDER, W. E. **A Capillary Tube Method for the Determination of the Coagulase Reaction.** *J. Lab. & Clin. Med.* 1959, May, v. 53, No. 5, 804–6, 1 fig.

To test staphylococcus cultures for coagulase, 1–1¼ mm. capillary tubes are used into which equal quantities of, first, 18-hour broth culture and, second, plasma are run. After 3-hours' incubation a "clot" can be seen at the interface if the strain is coagulase-positive. This test has been found to give good correlation with a conventional test [but the comparison is not reported in detail].

R. E. O. Williams

THOMAS, C. G. A. & PENIKETT, E. J. K. **Grading of Coagulase-Positive Staphylococci in the Control of Hospital Cross-Infection.** *J. Hygiene.* 1959, June, v. 57, No. 2, 162–73. [19 refs.]

Strains of *Staphylococcus pyogenes* isolated from routine cultures in Guy's Hospital have been divided into 4 grades A, B, C and D, according to a system of grading introduced by KNOTT and BLAIKLEY [this *Bulletin*, 1945, v. 20, 112]. Assignment to a grade depended upon coagulase production, lysin production, pigmentation and carbohydrate fermentation. In this study mannitol fermentation was the only carbohydrate degradation used in grading and was studied in detail, but difficulty was experienced in obtaining reproducible results.

Strains from patient and staff carriers, septic cases in maternity and burns units over a 2-year period were graded and compared. More than 70% of all strains and 84·9% of strains from septic cases in the maternity department belonged to grade A. [28% of strains from lesions were grade A in Knott & Blaikley's series 15 years ago]. There was no correlation between the grade of a staphylococcus and its production of diffusible antigens.

The difficulties of assigning a staphylococcus to a particular grade are discussed. The number of grades is less than the number of possible combinations of results, results or tests are not always reproducible and all produce quantitative differences. The authors conclude that strains from septic lesions are more likely to belong to grade A but that grading is not of practical use to the clinician as a measure of virulence.

M. Patricia Jevons

WOOD, R. C. & STEERS, E. **Study of the Purine Metabolism of** *Staphylococcus aureus*. *J. Bacteriology.* 1959, June, v. 77, No. 6, 760 65. [17 refs.]

YEGIAN, D., GALLO, Gloria & TOLL, M. W. **Kanamycin Resistant Staphylococcus Mutant requiring Heme for Growth.** *J. Bacteriology.* 1959, July, v. 78, No. 1, 10–12.

RICHOU, R., QUINCHON, C. & PANTALÉON, J. Recherches sur les agglutinines antistaphylococciques naturelles des sérums humains et animaux. [**Natural Anti-Staphylococcal Agglutinins in Sera of Man and Animals**] *Rev. d'Immunologie.* 1959, Jan.–Mar., v. 23, Nos. 1/2, 39–53.

The hypothesis of SLOCUM and LINDEN [this *Bulletin*, 1940, v. 15, 311] that enterotoxic staphylococci could be distinguished from others by their agglutinability in normal horse sera was tested with 45 strains from various sources. No relation could be found between agglutinability in horse, bovine or sheep serum and any other of a number of biological characteristics tested. [Human sera do not appear to have been tested in detail.]

R. E. O. Williams

MANN, P. H. **Comparison of the *in Vitro* Susceptibility of Strains of *Micrococcus pyogenes* var. *aureus* to Various Antibiotics.** *Antibiotic Med.* New York. 1959, June, v. 6, No. 6, 353–7.

100 coagulase-positive penicillin-resistant staphylococci isolated from clinical material were tested by the tube dilution method for sensitivity to tetracycline, bacitracin, oleandomycin and 1 : 2 combination of oleandomycin and tetracycline. They were also bacteriophage-typed.

Only 17% of strains were sensitive to tetracycline but 76–80% were sensitive to oleandomycin, the oleandomycin-tetracycline combination, and bacitracin.

Many strains were of the same phage type, one-third belonging to type 80 but it is not stated how many epidemics these strains represent. *M. Patricia Jevons*

SIPPE, G. R. ***Staphylococcus aureus* in a Rural Area of N.S.W.** *Med. J. Australia.* 1959, May 16, v. 1, No. 20, 666–9, 2 figs.

Of 550 strains of *Staphylococcus aureus* isolated from in- and out-patients attending a hospital in a small town in New South Wales, 26% were sensitive to penicillin, 77% to oxytetracycline, 89% to streptomycin and 94% to chloramphenicol. 96% of 278 were sensitive to erythromycin. In-patient strains differed little from out-patient strains. 72% of 43 strains proved to be type 80/81. *R. E. O. Williams*

CROWLEY, Nuala, with the technical assistance of R. MARTIN & J. PRESCOTT. **The Association of Starch-Accumulating Strains of Group A Streptococci with Acute Nephritis and Acute Rheumatic Fever.** *J. Hygiene.* 1959, June, v. 57, No. 2, 235–47, 3 figs. [15 refs.]

More than 600 strains of group A streptococci were divided into groups according to starch formation and subgroups depending on amylase production and conditions necessary for the production of starch.

The subsequent clinical history was known of patients from whom 469 strains were isolated at the beginning of respiratory tract infections. 35 strains came from patients who subsequently developed non-suppurative sequelae (21 acute nephritis; 7 acute rheumatism). All these strains formed starch, 29 of them in large amounts. 238 strains from patients not known to have developed complications did not form starch and 99 strains formed small amounts. Of 34 strains isolated near the onset of nephritis or rheumatic fever 29 were in subgroup *x* and readily accumulated starch, 4 were amylase producers of which 2 were also good starch producers.

Non-suppurative sequelae followed infections by 40% of the 175 starch-accumulating strains out of 579 strains tested, compared with 2·8% of all other strains in this group.

The type distribution of strains in Britain shows a high preponderance of some types including type 12 (47% of all T12 strains accumulate starch) in spite of this there is a correlation between starch accumulating strains, irrespective of serotype, and sequelae.

M. Patricia Jevons

SLADE, H. D. & KIMURA, Y. **Studies on *Streptococcus pyogenes*. IV. Effect of Whole Cells, M and C Antigens, and other Components of the Cell on Adrenalectomized Rats.** *J. Exper. Med.* 1959, June 1, v. 109, No 6, 589–600. [18 refs.]

Normal rats are very resistant to living mouse virulent group A streptococci. Adrenalectomized rats, however, were killed by $5{\cdot}3 \times 10^8$ organisms, by 30 times that number of mouse avirulent group A streptococci and 100 times the number of heat-killed organisms. The large number of organisms that were necessary to kill suggested the lethal effect was due to toxicity of the components.

Highly purified M protein prepared by sonic oscillation from strains of 4 serological types killed adrenalectomized rats but M preparations from strains extracted in hot acid were non-toxic. This toxicity was destroyed by trypsin and by pre-incubation of the preparation with homologous type-specific antiserum but not by heterologous antiserum. Rats injected with homologous antiserum 18 hours before the test preparations were not killed.

Highly purified C substance prepared from groups A, B, C and D by sonic extraction were toxic to adrenalectomized rats but that prepared by acid extraction was not toxic, this lethal effect was destroyed by pre-incubation with homologous group antiserum but unaffected by trypsin treatment.

Purified T28R preparations and nucleoprotein from a T19 strain were non-toxic as were proteins extracted from streptococci of groups B and D.

The toxic activity of the C and M preparations is shown to be destroyed by hot acid while the serological activity is not. The authors suggest that these 2 activities are functions of different parts of the molecules, rabbit antibody to the whole cell neutralizing both functions.

[For earlier parts see this *Bulletin*, 1956, v. 31, 864; 1957, v. 32, 201; 1958, v. 33, 173.]

M. Patricia Jevons

MATHESON, B. H. & REED, R. W. **Experimental Nephritis due to Type Specific Streptococci. III. Biological, Chemical and Physical Studies on Type 12 Nephritogenic Substance.** *J. Infect. Dis.* 1959, May–June, v. 104, No. 3, 213–32, 28 figs. [23 refs.]

The authors have previously shown [this *Bulletin*, 1955, v. 30, 173] that the intravenous injection of rabbits with culture filtrates of type 12 haemolytic streptococci from nephritic patients led to hypertension, albuminuria and sometimes haematuria. In the further experiments now reported, hypertension has been taken as the principal indicator response; albuminuria appeared to be relatively infrequent. Culture filtrate and dialysate were both active; the activity of the dialysate was abolished by heating to 100°C. for 15 minutes but not by 60°C. for 1 hour. The active fraction could be precipitated from the dialysate by saturated and by 50–75% ammonium sulphate. A similar fraction prepared from the dialysate of a type-17 streptococcus culture was inactive. Further fractional precipitation revealed that "all the type 12 polypeptides responsible for hypertension" are precipitated between 65 and

70%. These results were confirmed with a freshly isolated type-12 streptococcus from a patient with nephritis. Comparison of the purified fractions from the type-12 and type-17 streptococci by infra-red and ultra-violet absorption, ultracentrifugation, horizontal paper electrophoresis, and paper chromatography revealed no significant differences.

Illustrations are provided of single glomeruli from various rabbits. In association with the hypertension, changes of congestion and oedema of the glomeruli were seen and there were sometimes adhesions and proliferation of the capsular epithelium.

[In the earlier reports greatest stress was laid on the urinary changes; haematuria is barely mentioned in the present report and albuminuria was clearly irregular in appearance. Previously, microscopy of the kidneys was said to reveal tubular damage but little effect on the glomeruli; now the glomerular response is apparently the common one, though the photographs are not all very convincing. These major discrepancies between the 2 reports are not discussed.]

R. E. O. Williams

MAEKAWA, S. & HAYASHI, T. **Studies on the Hemolysin of Hemolytic Streptococci. V. The Influence of Potassium Ions and Ribonucleic Acid on the Formation of Streptolysin-S by Resting Streptococcal Cells.** *Japanese J. Microbiol.* 1958, Oct., v. 2, No. 4, 385–93, 5 figs. [12 refs.]

The streptolysin-S forming system, reported by BERNHEIMER [this *Bulletin*, 1950, v. 25, 407] containing ribonucleic acid, maltose, potassium dihydrogen phosphate and magnesium sulphate was re-examined with Group A *Streptococcus pyogenes* strain S No. 8. The optimum concentration of potassium ion ((K +) 0·4M) for streptolysin formation was much higher than that of phosphate ion (0·03 M). The process of streptolysin formation in the optimum system (*p*H 7·0) consists of an initial inhibition phase followed by a production phase after which the streptolysin activity is reduced. The initial inhibition phase is missing when the K + concentration is lower (0·03 M) or when the *p*H of the optimum system is adjusted to 6·0 units. Streptolysin production was enhanced by ammonium ions and suppressed by sodium ions when these ions partially replaced the K +. The amount of K+ transported into the cells from the medium containing a low concentration of KCl, producing small amounts of streptolysin, was unexpectedly higher than that from the medium containing a high concentration of KCl, in which a high titre of streptolysin was found.

H. Gooder

SORU, Eugenia & ISTRATI, Maria. Répercussion de l'inhibition monoenzymatique sur le complexe enzymatique de la cellule. L'action du sérum antistreptodornase sur le complexe enzymatique du streptocoque. [**Repercussions of Monoenzymatic Inhibition on the Enzymatic Complex of the Cell. Action of Antistreptodornase Serum on the Enzymatic Complex of the** *Streptococcus*] *Arch. Roumaines Path. Exper. et Microbiol.* 1959, Mar., v. 18, No. 1, 15–25, 8 figs.

SOUTHARD, W. H., HAYASHI, J. A. & BARKULIS, S. S. **Studies of Streptococcal Cell Walls. IV. The Conversion of D-Glucose to Cell Wall L-Rhamnose.** *J. Bacteriology.* 1959, July, v. 78, No. 1, 79–81. [13 refs.]

SMITH, Evelyn E. B., MILLS, G. T., BERNHEIMER, Harriet P. & AUSTRIAN, R. **A Study of some Enzymes in Extracts of a Non-Capsulated Strain of** *Pneumococcus* **concerned with Uridine Pyrophosphoglycosyl Metabolism.** *J. General Microbiol.* 1959, June, v. 20, No. 3, 654–69, 7 figs. [42 refs.]

Fractionation of extracts obtained from the non-capsulated strain R.19 of *Streptococcus pneumoniae* (derived from a strain of capsular type II) by disruption of cells in a Mickle disintegrator is described.

The uridyltransferases acting upon uridine pyrophosphoglucose (UPPG) and uridine pyrophosphoacetylglucosamine were partially separated. Uridine pyrophosphogalactose and guanosine pyrophosphomannose were not pyrophosphorylized. The extracts also contained uridine pyrophosphogalactose-4-epimerase and phosphogalactosyl uridyl transferase; these enzymes were involved in the conversion of galactose-1-phosphate to glucose-1-phosphate. Mannose was converted to glucose phosphate without the participation of UPPG.

Evidence is presented for the existence of a diphosphopyridine linked UPPG dehydrogenase capable of forming uridine pyrophosphoglucuronic acid (UPPGA) from UPPG. The epimerization of UPPGA to uridine pyrophosphogalacturonic acid which had previously been demonstrated in extracts of a capsulated strain of type 1 pneumococcus (SMITH *et al.*, *Biochim. Biophys. Acta.*, 1958, v. 29, 640) did not occur. The cellular content of UPPGA was observed not to reach significant amounts until the stationary phase of growth of the organism.

H. Gooder

BEISER, S. M., PAHL, H. B., ROSENKRANZ, H. S. & BENDICH, A. **Studies on the Fractionation of transforming Deoxyribonucleic Acid of Pneumococcus. I. Recovery and Dose-Response Relationships.** *Biochim. et Biophys. Acta.* 1959, Aug., v. 34, No. 2, 497–502, 2 figs. [16 refs.]

JACOTOT, H. & VALLÉE, A., with the technical collaboration of A. LE PRIOL. Sur un critère du pouvoir pathogène des brucelles. (Deuxième note.) [**A Criterion of the Pathogenicity of** *Brucella*] *Ann. Inst. Pasteur.* 1959, Jan., v. 96, No. 1, 54–9.

An extensive series of observations on the persistence of septicaemia in the guineapig after subcutaneous injection of suspensions of *Brucella* strains is presented.

The series included observations with the standard international strains of the *melitensis*, *abortus* and American *suis* types as well as many others in the *abortus* and *suis* categories.

All animals injected with standard strains showed high levels of persisting blood infection and associated splenomegaly.

There were, however, a number of vaccinal strains

which had become attenuated in subculture and were much less capable of producing septicaemia or splenomegaly. The contrast between strains of high and low pathogenicity was best appreciated by making blood cultures on inoculated groups of guineapigs from the 3rd to the 6th week after inoculation. *J. W. McLeod*

SIGNORINI, L. F. & GUERRA, M. Sui rapporti fra infezione brucellare. e infezione tubercolare. Ricerche sperimentali. [**Experimental Investigations on the relations between Brucellar and Tuberculous Infection**] *Ann. Sclavo.* Siena. 1959, Mar.–Apr., v. 1, No. 2, 215–32. [36 refs.] English summary.

Some experiments reported by other authors had pointed at the possibility that infection or vaccination either with *Mycobacterium tuberculosis* or with *Brucella* hindered the development of infection by the other micro-organism. Some tuberculous lesions in animals previously treated with *Brucella* appeared comparable to those produced by an attenuated tubercle bacillus. ELBERG *et al.* [this *Bulletin*, 1958, v. 33, 195] demonstrated a cross immunity in monocytes *in vitro*. In guineapigs interference was noticed between brucellosis and Q fever [*Trop. Dis. Bull.*, 1959, v. 56, 293], probably comparable to interference between viruses. Workers are quoted who concluded that interference between brucellosis and tuberculous infection depended on cellular immunity, though stimulation of the reticulo-endothelial system could also play a part.

The authors studied the development of tuberculosis in guineapigs which had been treated with *Brucella* in various ways—by infection with a virulent and with an attenuated strain of *Br. abortus*, and by vaccines prepared and administered in different ways. In a preliminary experiment 14 groups of 5 guineapigs were used. 1 animal received only the treatment with the *Brucella* preparation. A month after the end of the treatment the other 4 were infected with 5 mgm. of a human strain of *Myco. tuberculosis*. Survival times were slightly shorter in those treated with live virulent *Br. abortus*, and no longer than in the controls in those treated otherwise, except in the group which had been treated with the live attenuated *Br. abortus* strain (Buck 19), although, as expected through the small numbers used, the difference was not significant. The same result was obtained when the weight of the spleen was taken as an index of the extent of tuberculous infection.

In the second experiment 2 groups of 11 guineapigs each were inoculated with a live attenuated strain of *Br. abortus* (Buck 19), subcutaneously and intravenously respectively, one animal being left uninfected with *Myco. tuberculosis*. Guineapigs were allowed to die naturally. All animals, in fact, died of the tuberculous infection given them, but the treated ones survived for a significantly longer period (83·3 days for those treated subcutaneously and 84·2 for those treated intravenously, on an average, compared with 62·4 for the controls). In no case could *Brucella* be cultivated from the organs. A hypothesis put forward suggests that the attenuated *Brucella* stimulates the non-specific defence forces of the body, especially those of the reticulo-endothelial system. *E. Agius*

TAKETA, S., ITO, M. & ONO, Y. **Experimental Studies on the Passive Transfer of *Yato-byo* (Tularemia of Japan) Hypersensitivity. I.** *Fukishima J. Med. Sci.* 1957, v. 4, No. 2, 107–12, 1 fig. [11 refs.]

The inoculation of killed *Yato-byo* bacilli into normal guineapigs was found to induce a delayed cutaneous hypersensitivity of the tuberculin type, and it was decided to attempt passive transfer of this allergic response. Serum of sensitized guineapigs did not induce hypersensitivity when injected into normal guineapigs. Leucocytes of sensitized animals were harvested from sterile peritoneal exudates and injected intraperitoneally into normal guineapigs; 48 hours later these recipient animals were shown to have developed marked cutaneous response to *Yato-byo* antigen. Similar results were obtained when lymph-node emulsions were transferred from sensitized to non-sensitized guineapigs. Rather surprisingly, transfer of hypersensitivity was almost equally effective when washed peripheral blood cells from sensitized guineapigs were injected into normal animals.

[This appears to be a preliminary report, and no experimental analysis or discussion of the findings is presented. In general the results conform with those obtained by CHASE (*Proc. Soc. Exper. Biol. & Med.*, 1945, v. 59, 134) on cellular transfer of tuberculin hypersensitivity.] *Derek Hobson*

BROWN, Annie M. **Growth Idiosyncrasies of some *Bordetella pertussis* Strains, and the Intracerebral Virulence of these Strains in Mice.** *J. General Microbiol.* 1959, June, v. 20, No. 3, 532–9, 5 figs. [10 refs.]

"The growth characteristics of eight strains of *Bordetella pertussis* were studied in defined liquid media. Two of these strains (1017, 1018), which are both very virulent on intracerebral injection into mice, were found to have growth idiosyncrasies. Both these strains differed from typical virulent pertussis strains and from a degraded strain in that they needed more magnesium and a different gas phase (carbon dioxide and oxygen) for optimal growth in defined liquid medium. Both strains were inhibited by crystalline lysozyme (100 mg./ml.) in defined medium, whereas typical virulent strains and a degraded strain were insensitive to it."

YAMAMOTO, A., GOMIBUCHI, A., ZEN-YOJI, H., KIKUCHI, T. & TANAKA, T. **Studies on *Hemophilus pertussis*. XII. On the Similarity between the Capsular Antigen and Skin Test Antigen.** *Japanese J. Microbiol.* 1958, Oct., v. 2, No. 4, 395–401. [15 refs.]

"1) With the skin test antigen extracted from pertussis cells by heating in acid (pH 1.8) and through ammonium sulfate and picric acid precipitation, an absorption test was performed on pertussal capsular (K) and somatic (O) antigen to investigate the identity or differences between these antigens.

"2) The skin test antigen completely absorbed K antibody in *H. pertussis* antiserum, but when heated at 100°C for 30 minutes, it lost the absorbing power.

"3) The skin test antigen did not absorb O antibody

in the above mentioned antiserum, proving non-relation between the two."

De Caro, M. & Samarani, Elena. Il fattore istaminosensibilizzante del vaccino antipertossico. [**The Histamine Sensitizing Factor in Pertussis Vaccine**] *Rendiconti Istituto Superiore di Sanità.* Rome. 1959, v. 22, Pt. 4, 379–90. [25 refs.] English summary.

This is a study to determine the factor present in pertussis vaccine which lowers the resistance of mice to histamine (the histamine sensitizing factor, or HSF), of the effect of temperature on it, and of the role of the adrenals in this connexion.

The minimum lethal dose of histamine hydrochloride for Swiss mice was found to be 1,500 mgm. per kgm. body weight. With a vaccine dose equal to 2,500 million *H. pertussis* a 10-fold increase in sensitivity was produced, young mice being more resistant. After a vaccine dose of 10,000 million *H. pertussis* micro-organisms 100% mortality followed the administration of 1/10 of the ordinary MLD of histamine. Exposure of the vaccine to 60°C. for 30 minutes did not affect the HSF, which was destroyed by 80°C. for the same time.

Bilateral adrenalectomy by itself was found to render most mice sensitive to one-tenth of the MLD of histamine, a change which was not attributable to operative trauma. A group of mice were found, discordantly, to have become sensitive to as little as 1/100 of the MLD. Studies involving adrenalectomy are complicated by the possible occurrence of accessory suprarenals, which some authors report as being found in as many as 49·6% of mice. The HSF is present only in bacteria in phase I.

It is not possible to link the greater case mortality of whooping-cough in females than in males with any action of the HSF. From the table given this difference in 5 years in Italy was never more than about 20% (*e.g.* 0·9% for males, 1·1% for females). From the point of view of human prophylaxis, the fact that the mouse is abnormally sensitive to pertussis vaccine, that children would react rather like the normally resistant rabbits and guineapigs, that the sensitizing dose would be relatively much larger than those normally employed, and that this effect is transitory, would make the role of HSF one which need not be viewed with special apprehension. *E. Agius*

Iida, T., Taguchi, M., Kimura, H. & Komase, Y. **Further Studies on Variants of** *Haemophilus pertussis*: **Electronmicroscopic Observations and the Property of Histamine Sensitization of Mice.** *Japanese J. Microbiol.* 1958, Oct., v. 2, No. 4, 351–6, 7 figs. [19 refs.]

Stuy, J. H. **Studies on the Radiation Inactivation of Microorganisms. V. Deoxyribonucleic Acid Metabolism in Ultraviolet-Irradiated** *Haemophilus influenzae. J. Bacteriology.* 1959, July, v. 78, No. 1, 49–58, 7 figs. [18 refs.]

Wiener, S. L., Tinker, Mary & Bradford, W. L. **Experimental Meningoencephalomyelitis produced by** *Hemophilus pertussis. Arch. Pathology.* 1959, June, v. 67, No. 6, 694–9, 4 figs. [13 refs.]

"Experimental encephalomyelitis has been produced in the Hartley strain of guinea pig by the intracutaneous injection of an adjuvant antigen containing rabbit spinal cord, paraffin oil, an emulsifying agent, and killed Hemophilus pertussis.

"The lesions produced were predominantly meningeal and perivascular and, though less severe, resembled those produced by a similar antigen containing killed Mycobacterium tuberculosis."

Albrecht, J. & Husmann, K. H. Die Chemotherapie der experimentellen Infektion mit *Haemophilus pertussis* [**The Chemotherapy of Experimental Infection with** *Haemophilus pertussis*]. *Arch. f. Hyg. u. Bakt.* 1959, Aug., v. 143, No. 5, 366–78. [70 refs.]

In this paper there is first a critical review of the extensive literature on the problems of experimental pertussis infection and the results obtained by various workers in the chemotherapy of such infection. A detailed account is given of the work carried out by the authors to test the efficacy of the treatment by a number of antibiotics and other substances (a table gives particulars of these) of groups of 9–11 mice which had been infected with *Haemophilus pertussis* ("Hansen" strain) by intranasal instillation.

The main statistically significant results were that the survival time of infected mice was prolonged by treatment with various tetracyclines, chloramphenicol, streptomycin or neomycin but was not prolonged by spiramycin, novobiocin, polymyxin B, isoniazid, vitamin C or vitamin K.

There is a long discussion of the findings.

M. E. Delafield

Smith, J. L. & Higuchi, K. **Studies on the Nutrition and Physiology of** *Pasteurella pestis.* **IV. Utilization of Peptides during the Growth of** *Pasteurella pestis. J. Bacteriology.* 1959, May, v. 77, No. 5, 604–8, 3 figs. [22 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1027.]

Power, D. A. & Pelczar, M. J., Jr. **Growth Enhancement of the Reiter Treponeme by Fatty Acids.** *J. Bacteriology.* 1959, June, v. 77, No. 6, 789–93, 2 figs. [20 refs.]

"Growth of the Reiter treponeme in a spirolate broth plus 10 per cent inactivated sheep serum medium supplemented with TEM 4T (the diacetyl tartaric acid ester of tallow monoglycerides) at a concentration of 0.20 to 0.25 mg per ml results in a cell crop 2 to 3 times as large as that obtained without the fatty acid supplement. The TEM 4T can be replaced by a mixture of palmitic, stearic, and oleic acids, in equal amounts, and at a total fatty acid concentration of 0.20 to 0.25 mg per ml of the medium."

De Bruijn, J. H. **Investigations into the Antigenic Structure of the Reiter Strain of *Treponema pallidum*. II. The Complex Nature of the Protein Fraction.** *Antonie van Leeuwenhoek: J. Microbiol. & Serol.* 1959, v. 25, No. 1, 41–5.

This is a continuation of a previous article [this *Bulletin*, 1959, v. 34, 494] 15 ml. of protein antigen (Reiter), 5 mgm. trypsin and 0·15 ml. of 1% merthiolate [thiomersal] solution were mixed; the *p*H was adjusted to 8·5 with 0·1 N NaOH and the whole incubated at 37°C. for 4 days; after 2 days from the start 5 mgm. more of trypsin were added. The whole was centrifuged, the deposit discarded and 40·5 ml. absolute ethanol added to the supernatant; after the precipitate had settled all night at 5°C. it was centrifuged and dissolved in 15 ml. of normal saline.

A rabbit was immunized with a series of 5 injections of protein antigen and bled on the 18th day; the resulting serum was heated for 30 minutes at 61°C.

Complement-fixation tests on syphilitic serum with heated and unheated protein antigens showed that heated antigen gave negative results; however, the anti-protein-antigen rabbit serum still reacted with heated antigen and from this it was assumed that the nature of the antigen was polysaccharide. When anti-protein-antigen serum was titrated with the heated and unheated lipopolysaccharide component, results were not appreciably affected in the higher dilutions but in the lower ones a heat-labile factor seemed to be active, presumably due to lipoid. Thus the protein fraction of the Reiter spirochaete seems to be a lipopolysaccharide-protein complex, but the polysaccharide part does not interfere with serodiagnosis of syphilis because there is no corresponding antibody in syphilitic serum.

T. E. Osmond

Kirschner, L. & Graham, L. **Growth, Purification and Maintenance of Leptospira on Solid Media.** *Brit. J. Exper. Path.* 1959, Feb., v. 40, No 1, 57–60, 4 figs. on pl.

The solid medium used in the experiments reported here is essentially the same as that described by Cox and Larson [this *Bulletin*, 1957, v. 32, 999] except that it contained in addition 2,6-dichlorphenol indophenol in a concentration of 1/30,000 as an oxidation-reduction indicator, and 1 μgm./ml. of either vitamin B12 or B1. The medium was distributed into narrow test tubes and small petri dishes; the former were inoculated as stab cultures, and the surface of the plate cultures was either spotted with single drops of fluid culture or one drop (containing 20,000–40,000 leptospires) was spread over the surface to produce isolated colonies.

In stab cultures the typical rings of growth, situated 5–10 mm. below the surface, appeared during the second week of incubation but, if a bacterial contaminant was present, growth throughout the whole column with marked reduction of the indicator was visible after a day or two. These cultures therefore provided a good means of checking the purity of the leptospiral strains.

Viable leptospires were still present in cultures stored for 6 months (the longest period of observation) at either 17°C. or at 6–10°C.

On plate cultures spreading circles of growth developed below the surface of the medium; the rates of growth differed widely from one strain to another, and the diameters of the colonies formed ranged from 10–40 mm. Any bacterial contaminants present in a culture (usually staphylococci or yeasts) produced circumscribed colonies easily differentiated from the leptospiral elements by their appearance. Pure cultures of leptospires could generally be obtained by cutting a small piece of medium from the periphery of the circle of growth and transferring it to normal liquid medium.

The authors claim that the medium offers 2 advantages: it reduces the frequency of subculturing in routine maintenance of strains of leptospires, and it provides a simple means of purifying contaminated cultures.

J. C. Broom

Faine, S. **Iron as a Growth Requirement for Pathogenic Leptospira.** *J. General Microbiol.* 1959, Apr., v. 20, No. 2, 246–51. [14 refs.]

Most of the media used for the cultivation of pathogenic leptospires contain a small quantity of haemoglobin either as a solution or in the form of laked erythrocytes, but little is known about its mode of action. This article describes the results of experiments carried out in an attempt to obtain information on that question. A batch of Korthof's culture medium was prepared containing rabbit serum which was collected with special care to avoid haemolysis. Analysis showed the iron content to be 40 μgm. Fe/100 ml. whereas a medium which gave good growth had about 190 μgm. Fe/100 ml. In the 40 μgm. medium, no visible growth occurred unless a heavy inoculum of at least 10^7 organisms/ml. was used. With such an inoculum, growth could be discerned if the medium provided sufficient nutriment to allow 4–5 generations of leptospires to develop.

Supplements were added to give about 10^{-4}M final concentrations of the following: haemoglobin (1) untreated, (2) heated at 56°C., (3) boiled; carboxyhaemoglobin; methaemoglobin; haematin; $FeCl_3$. Duplicate tubes, which contained 1 ml. of the various media, were each seeded with 10^4 *Leptospira icterohaemorrhagiae* and the degree of growth determined by direct counts after incubation at 30°C. for 4, 7 and 18 days.

Large numbers of leptospires were still present after 18 days in the tubes containing untreated haemoglobin, haematin or $FeCl_3$ but [so far as can be made out from the author's table] good growth occurred only for the first few days in tubes containing the other supplements and the cultures had died out by the 18th day.

Other experiments with untreated haemoglobin and $FeCl_3$ showed the optimum concentration to be equivalent in each case to about 10^{-5}M-Fe, but growth was faster in the haemoglobin cultures.

Little is known of the enzymes present in leptospires, but Fulton and Spooner [this *Bulletin*, 1956, v. 31, 865] demonstrated the presence of a cytochrome-*c* system, and the present author found catalase in some strains of certain serotypes (*Proc. Univ. Otago Med.*

School, 1958, v. 36, 27). He suggests that iron porphyrin compounds derived from haemoglobin provide the most effective precursors for the synthesis of these enzymes. *J. C. Broom*

FUCHS, G. H. P. Beiträge zur Leptospirenzüchtung. I. Mitteilung. Untersuchungen über die Brauchbarkeit des Rinderaugen-Glaskörpers und des Regenwassers als Grundsubtrat für die Leptospirenkultur. [**Contributions to the Cultivation of Leptospira. I. Communication. Investigations on the Use of Bovine Vitreous and of Rain Water as Basic Substrate for the Cultivation of Leptospira**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos 7/8, 601–15, 1 fig. [41 refs.]

In a series of experiments the author found that pathogenic leptospires would grow in a medium containing vitreous humour obtained from the eyes of cattle. When dilutions were made in basic Korthof's medium (without rabbit serum) the optimum concentration of vitreous was 33%; in pure rain water without salts the optimum was 50%. Sheep serum could also act as a substitute for rabbit serum, the best concentrations with the 2 diluents being 20% and 33% respectively. *J. C. Broom*

GOLDBERG, H. S. & ARMSTRONG, J. C. **Oxidase Reaction with Leptospiral Colonies and its Adaptation to Antibiotic Sensitivity Testing.** *J. Bacteriology*. 1959, Apr., v. 77, No. 4, 512–3, 2 figs.

Leptospires can be grown on the solid medium described by COX and LARSON [this *Bulletin*, 1957, v. 32, 999] but morphological observation on the appearances of the colonies are difficult because of their transparency. Tests were made to determine whether dyes or other reagents would be taken up selectively by the leptospiral colonies and thereby increase their visibility, and it was found that the standard oxidase reagent, *p*-aminodimethylaniline, gave rapid, clear typical results.

Leptospiral colonies gave a positive oxidase reaction, showing a deep pink coloration within 2 minutes of the addition of the reagent while the medium remained colourless. After some hours the colonies became maroon, brown and black. 5 morphologically different types of colony could be identified and are being further studied.

On the basis of these observations an antibiotic disk sensitivity test was developed. Plates, heavily inoculated with leptospires, were incubated for 48 hours, then antibiotic disks were put in place and the cultures incubated for a further 24 hours. When the reagent was added, zones of inhibition were visible around disks containing antibiotics to which the leptospires were sensitive.

Most of the work was carried out with *Leptospira biflexa* but similar results were obtained with 7 [unnamed] pathogenic serotypes. Further work is being carried out to standardize the test for the routine investigation of possible antileptospiral compounds. *J. C. Broom*

VARFOLOMEYEVA, A. A. **The History of the Discovery, the Characteristics and Nomenclature of the Cause of Leptospirosis,** *Leptospira monjakow*. *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 8, 1214–19, 3 figs. [15 refs.] [Translated from Russian.]

The author emphasizes the confusion which can arise when authors give names to strains of leptospires which they have isolated, without comparing their serological characters with those of serotypes already established. As an illustration she relates some of the history of the serotype which is commonly known in the U.S.S.R. as *Leptospira monjakow* [though the name is sometimes transliterated differently] but which was shown by KMETY *et al.* to be identical with *L. pomona* [this *Bulletin*, 1957, v. 32, 442]. The original strain, isolated in 1937 by TERSKIKH and named after the patient, was sometimes known also as *L. typi II*. A serologically identical strain was isolated from cattle in 1939 by ZEMSHOV and VORONEZH but was named *L. icterohaemoglobinuria*. Then in 1941 KIKENKO and ANAN'IN named similar strains Far East Type B (shortened to DV-B). Next LUBASHENKO in 1946 proposed *L. icterohaemorrhagiae animalis* or *L. icteroanemiae* for the causative agent of leptospirosis in silver foxes.

Thus, within a few years the serotype had acquired 6 different names.

The author made a large series of cross-agglutination tests, comparing the U.S.S.R. strains with strains of *L. pomona* obtained from a number of other workers. She concluded that all the strains were serologically identical, and therefore proposes that the names used in the U.S.S.R. should be regarded as synonyms of *L. pomona*. *J. C. Broom*

ALEXANDER, A. D., EVANS, L. B. & KEEN, B. C., Jr. *Leptospira butembo;* **a Distinct Leptospiral Serotype.** *J. Bacteriology*. 1959, May, v. 77, No. 5, 668–9.

A full serological study was made of the Butembo strain of leptospires originally isolated from a human patient in the Belgian Congo by VAN RIEL [*Trop. Dis. Bull.*, 1947, v. 44, 320]. Agglutination tests showed that the strain had minor antigenic relationships with *Leptospira grippotyphosa* and members of the Autumnalis serogroup, and rather closer affinities to *L. cynopteri*. Cross-absorption tests proved, however, that strain Butembo represents a new serotype for which the name *Leptospira butembo* is proposed. *J. C. Broom*

CASELITZ, F. H. Grundsätzliche Erwägungen über den *Vibrio jamaicensis* (Vorkommen, Klassifizierung, Verwandtschaft). [**Basic Considerations on** *Vibrio jamaicensis*] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 3/4, 238–43. [12 refs.]

The author, who has already written on the subject of this *Vibrio* [this *Bulletin*, 1957, v. 32, 503, *bis*; 1958, v. 33, 615], draws attention to the fact that its incidence is not limited to tropical climates. It has been found in urine, faeces, bile, sputum and in a patient with osteomyelitis in Germany.

There is difficulty in adopting a rigid morphological

criterion of classification and it is considered that, on account of the production of both acid and gas in the fermentation of glucose, these micro-organisms should be grouped in the genus *Aeromonas* within the family pseudomonadaceae. *J. W. McLeod*

De, S. N. **Enterotoxicity of Bacteria-Free Culture-Filtrate of** *Vibrio cholerae.* [Correspondence.] *Nature.* 1959, May 30, v. 183, 1533–4.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1028.]

Schramm, G. & Mohr, Elisabeth. **Purification of Neuraminidase from** *Vibrio cholerae.* [Correspondence.] *Nature.* 1959, June 13, v. 183, 1677–8.

Berg, M. & Levinson, S. A. **Hyperglycemia and Histochemical Changes induced in Dogs by** *Clostridium perfringens* **Toxin.** *Arch. Pathology.* 1959, July, v. 68, No. 1, 83–93, 7 figs. [25 refs.]

Kujumgiev, I. Eine einfache Methode zur raschen Unterscheidung der *Listeria monocytogenes* von *Erysipelothrix rhusiopathiae.* [**A Simple Method for the Rapid Differentiation of** *Listeria monocytogenes* **and** *Erysipelothrix rhusiopathiae*] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 174, Nos. 3/4, 282–6. [14 refs.]

It is maintained that, although the differentiation of *Listeria monocytogenes* and *Erysipelothrix rhusiopathiae* can be clearly made by morphological, cultural, biochemical and immunological characters, this may prove cumbersome. A clear and sharp differentiation is obtained, however, by inoculating 2 drops of a 48-hour culture of these bacteria to 4 ml. of broth containing 0·01 ml. of a 2·5% solution of Prontosil (Bayer product). This medium is raspberry red in colour and is completely reduced by *L. monocytogenes* within 24 hours at 37°C., but remains unchanged in colour after 10 days where *E. rhusiopathiae is inoculated.* It is recommended that the reaction of the medium should be *p*H 7·4 for *L. monocytogenes* and *p*H 8·0 for *E. rhusiopathiae.*
J. W. McLeod

King, Elizabeth O. **Studies on a Group of Previously Unclassified Bacteria associated with Meningitis in Infants.** *Amer. J. Clin. Path.* 1959, Mar., v. 31, No. 3, 241–7.

24 strains of a new organism isolated over 7 years in 7 states of the U.S. have been examined. Of these strains 18 were isolated from either the cerebrospinal fluid or blood of infants with septicaemia or meningitis, 5 from throats of healthy infants (later treated with antibiotics) during a nursery outbreak of meningitis, and 1 from the throat of a healthy adult.

The characters of the organism are: Gram-negative, slender, slightly curved rod, with occasional clubbing and filaments, non-sporing, capsule varying, non-motile. The organism grew at 25°C. and 37°C. giving smooth, entire, grey-white, glistening, butyrous, non-haemolytic colonies, 1–1·5 mm. in diameter after 24 hours on 5% rabbit-blood, heart-infusion agar: a yellow pigment developed after 1 month on heart-infusion agar. There was no growth on S S agar and only with repeated subculture did growth take place on MacConkey agar. Only occasional strains grew on Simmons citrate agar.

The biochemical behaviour was as follows: oxidative utilization of glucose, lactose, laevulose, mannitol, mannose, trehalose, maltose took from 1–3 weeks; catalase +; oxidase +; urease −; indole + (weak); H_2S + (lead acetate papers only); gelatin +; litmus milk, alkaline and peptonized; NO_3 −; MR −; VP −. 23 strains were resistant to chlortetracycline, bacitracin, penicillin, polymyxin B and oxytetracycline: the strains tested against viomycin (14), neomycin (17), tetracycline (7), nitrofurantoin (7) were resistant; only 2 strains were sensitive to streptomycin (100 μgm./disk). There was varying sensitivity to chloramphenicol, carbomycin, magnamycin and erythromycin.

Antigenically there are 3 serological groups in the 24 strains. The organisms were non-pathogenic for rabbits (intravenous injection), for hamsters (subcutaneous injection), and of doubtful pathogenicity for mice (intracerebral and intranasal injection). The name *Flavobacterium meningosepticum* has been suggested for this organism. Representative strains have been given to the American Type Culture Collection—Ref. no. 13,253, 13,254 and 13,255—and to the National Collection of Type Cultures—Ref. no. 10,016.
Elizabeth M. Harper

FUNGI

Morenz, J. Ein Desoxycholatmedium zur Isolierung pathogener Pilze. [**A Desoxycholate Medium for the Isolation of Pathogenic Fungi**] *Ztschr. f.d.g. Hyg. u. ihre Grenzgebiete.* Berlin. 1959, Mar.–Apr., v. 5, No. 2, 102–6.

The medium described is similar to Littman's ox gall medium [this *Bulletin*, 1947, v. 22, 802] with the ox gall replaced by sodium desoxycholate at 50 mgm.%, and had the following composition:

1% dextrose
1% mycopeptone A (Atarost, Rostock)
0·1% yeast extract, without NaCl (Bramsch, Dresden)
2–2·5% Agar (without special *p*H adjustment).
To this medium, melted and cooled, were added:
50 mgm.% sodium desoxycholate (Schuchardt, Munich)
5 mgm.% streptomycin
2,000 units % penicillin. *G. C. Ainsworth*

Blank, H., Sagami, S., Boyd, Carolyn & Roth, F. J., Jr. **The Pathogenesis of Superficial Fungous Infections in Cultured Human Skin.** *Arch. Dermat.* 1959, May, v. 79, No. 5, 524–35, 11 figs. [30 refs.]

In a clearly written and well illustrated article these authors have recorded experiments and observations which would appear to indicate that normal human serum may be an important factor in determining the restricted distribution of dermatophytes in the lesions

which they cause. Having first established that certain species were reluctant to grow in a tissue-culture medium in spite of the presence in this medium of nutrient substances adequate for their growth, they proceeded to carry out further investigations in order to elucidate this phenomenon. It soon became clear that the main factor which inhibited the growth of the dermatophytes in this medium was human serum. This fungistatic effect of serum had been demonstrated previously by several workers whose work was, however, unknown to these authors when they commenced their present series of experiments and observations.

In the course of this work it was found possible to grow full-thickness pieces of human skin on various liquid and agar media. The normal human skin used for this purpose was the prepuce obtained at circumcision and naturally infected adult skin was obtained from clinically typical lesions. Prior to their being used, these pieces of skin were stored in Hanks medium to which had been added the antibiotics neomycin (500 μgm. per ml.) and bacitracin (500 units per ml.). Experimental sections were prepared from this material by slicing off, parallel to the surface of the skin, a top layer 0·5 mm. thick (which included the epidermis and a thin layer of dermis) using a "cold-sterilized Stadie-Riggs microtome". These slices were then placed immediately on the appropriate media dermal side down.

On both liquid and agar media these pieces of skin grew well and mitoses were observed in the epidermis even after 4 weeks of continuous culture. Moreover, it was found that pieces of skin grew surprisingly well on Sabouraud's agar. When such pieces of skin were inoculated with mycelial pellets of *Trichophyton rubrum* and *T. mentagrophytes* these fungi grew profusely, invading not only the stratum corneum but also the underlying tissues including the dermis. When a nutrient agar containing 50% or more of serum was inoculated with pellets of these dermatophytes their growth was strongly inhibited, and when pieces of skin were placed on such serum-containing media and inoculated with these dermatophytes, their growth in the skin was restricted to the stratum corneum. Decreasing concentrations of serum in the medium permitted correspondingly deeper invasion. Of great interest was the greater power of invasion exhibited by *T. rubrum*, an observation which is in accordance with its reputed behaviour *in vivo*.

The authors conclude from these observations that the restriction of the distribution of dermatophytes *in vivo* to keratin-containing tissues is probably not due to a special affinity on their part for such tissues but to the fungistatic action of certain as yet unidentified constituents of normal serum in the underlying tissues which prevents their becoming invaded by dermatophytes. *C. J. La Touche*

KARASAKI, T. **Studies on the Blood Concentration of Trichomycin. VI. The Therapeutic Blood Concentration for Experimental Candidiasis in the Rabbit.** *Antibiotics & Chemotherapy.* New York. 1959, June, v. 9, No. 6, 337–48, 3 figs.

Rabbits received a small inoculum of *Candida albicans* intravenously and were treated with the anti-fungal antibiotic trichomycin. They were killed 10 days later, the result being judged by the presence or absence of renal abscesses and by quantitative culture of kidney homogenate. It has previously been shown that the blood of some animals inactivates trichomycin. Such animals (whose blood contained no detectable antibiotics even immediately after an intravenous dose) were unaffected by the treatment. In rabbits not behaving in this peculiar way the infection was suppressed by adequate doses: these were 1,200 units per kgm. intravenously or 6,000 units per kgm. intraperitoneally: intramuscular injection had no effect. Several doses and systems of dosage were used and details of the effects are given, including the blood levels produced: at least 2–3 units/ml. seems to have been necessary for full fungistatic effect (the trichomycin used had a potency of 5,750 units per mgm.).

[For Part V, see this *Bulletin*, 1958, v. 33, 1075.]

L. P. Garrod

GORDON, M. A. **Fluorescent Staining of *Histoplasma capsulatum*.** *J. Bacteriology.* 1959, June, v. 77, No. 6, 678–81, 5 figs. [16 refs.]

"Fluorescein-labeled globulin derived from rabbits infected with *Histoplasma capsulatum* was found capable of differentiating this species by cellular stain from tissue forms of other human pathogens, including *Blastomyces dermatitidis*, *Cryptococcus neoformans*, *Sporotrichum schenckii*, and *Leishmania donovani*, *Coccidioides immitis* exhibited striking autofluorescence in the tissue phase. *Histoplasma duboisii* and a duboisioid strain of *H. capsulatum* were peculiar in that only the small buds fluoresced, to the exclusion of more mature cells. Strains of *Blastomyces brasiliensis* reacted similarly."

MARIAT, F. & GARDINI-TUESTA, W. E., with the technical collaboration of J. SATRE. Pouvoir pathogène expérimental d'une souche d'*Histoplasma capsulatum* isolée du singe africain. [**Experimental Pathogenicity of a Strain of *Histoplasma capsulatum* isolated from African Monkeys**] *Ann. Inst. Pasteur.* 1959, June, v. 96, No. 6, 669–79, 1 text fig. & 7 figs. on pl.

So far, altogether 7 cases of spontaneous histoplasmosis in African monkeys (*Cynocephalus babuin*) have been recorded in Paris since the first case was observed in 1955. These monkeys died sooner or later after their arrival but death was probably not due to histoplasmosis. All were in various degrees of cachexia on arrival and were heavily infested with worm parasites. The lesions in which the yeast phase of *Histoplasma* was observed were either cutaneous or subcutaneous, and, apart from enlargement of the axillary and inguinal glands no other lesions were found which could be attributed to infection by this fungus. The yeast phase, which was found abundantly in the pus of ulcerated cutaneous lesions, consisted only of large thick-walled cells resembling those described as characteristic of *H. duboisii* by VANBREUSEGHEM [this *Bulletin*, 1953, v. 28, 628].

With this fungus the authors carried out a number of experimental inoculations of laboratory animals: guineapigs, hamsters and mice; the guineapigs being inoculated intra-testicularly and the hamsters and mice mainly intraperitoneally. In these animals the parasite generally remained localized in the site of inoculation; the testicle in the guineapig or in the case of the hamsters and mice in the organs in the immediate vicinity of the inoculation site. Exceptions to this were found in a guineapig and a hamster, in both of which animals cutaneous and subcutaneous lesions developed; also in two hamsters the yeast phase was observed in some of the viscera in which no major lesions had occurred: and in these 2 hamsters a further feature of note was the presence of gummata on the feet in which the yeast phase was present in abundance. In none of these animals nor in the spontaneously infected monkeys was the small form of the yeast phase observed. The authors conclude from these observations that, the pathogenicity of this variety of *Histoplasma* is generally of a very low grade in so far as it affects the animals which they have studied.

C. J. La Touche

Levaditi, J. C., Drouhet, E., Segretain, G. & Mariat, F. Sur le caractère histiocytaire de l'histoplasmose à petites formes et le caractère gigantocellulaire de l'histoplasmose à grandes formes. **[Histiocyte Reaction in "Small-Form" Histoplasmosis and Giant-Cell Reaction in "Large-Form" Histoplasmosis]** *Ann. Inst. Pasteur.* 1959, June, v. 96, No. 6, 659–68, 4 figs. [16 refs.]

A foreign body type of granuloma reaction of the infected tissues takes place whether histoplasmosis is spontaneous in origin or is experimentally induced. The nature of the cells taking part in this reaction appears to vary according to the size of the yeast phase of the parasite. Thus, in histoplasmosis of the classical type, in which small budding cells represent the yeast phase, the granuloma is composed of histiocytes containing the parasite, whereas in the African form of histoplasmosis in which the yeast phase is characteristically large, the granuloma is composed of multinucleate giant cells containing the parasite. It has been observed, moreover, that in most animals experimentally infected with the African form, the parasite reproduces itself in the early stages of infection by means of small cells and likewise when the infection runs an acute course, and that correspondingly, the reaction is of the histiocyte type, whereas in the later stages of infection or when the infection runs a chronic course, the yeast cells become successively larger, and accordingly the cellular reaction favours the formation of giant cells.

There is, however, an exception to this pattern of response; it is found in the experimentally infected mouse. Here large cells may be observed both in the giant cells and in wandering macrophages. In the mouse also a necrotic or an inflammatory response occurs more frequently than in other experimentally infected animals in lesions which are slow to develop.

C. J. La Touche

Hill, G. A. & Marcus, S. **Resistance induced against *Histoplasma capsulatum*: Quantitative Aspects.** *J. Infect. Dis.* 1959, July–Aug., v. 105, No. 1, 26–30. [12 refs.]

This is a statistically analysed quantitative comparison of the degree of resistance to infection by *Histoplasma capsulatum* engendered by 2 different methods, *viz.* (a) by means of a killed vaccine, and (b) by means of induced sublethal chronic infection. The LD50 in adult albino mice was first determined for 2 strains of *H. capsulatum* (6651 and G 17 M) and the tabulated results show that strain 6651 was less virulent than strain G 17 M. Tests extending over a 4-year period had shown that the LD50 of these 2 strains had not changed significantly. Groups of mice were then immunized by intraperitoneal injection of the formalin-killed yeast phase of the 2 strains of *H. capsulatum* used for the LD50 determinations, each animal receiving two injections one week apart. 30 days later randomly selected animals from the 2 groups of mice (*i.e.*, that vaccinated with strain 6651 and that vaccinated with strain G 17 M) were challenged intravenously with varying numbers of yeast-phase strain G 17 M organisms.

The results, which are tabulated and analysed by the method of Litchfield and Wilcoxon (*J. Pharmacol. & Exper. Therap.*, 1949, v. 96, 99), include the LD50 estimates and the potency ratio (that is, the ratio of the LD50 for the control and infected groups). At the same time a group of normal mice received the same challenge inoculum and the results are included in the table made out for the vaccinated mice. This table shows that the vaccinated mice were resistant to 1·2–23 times the number of organisms which killed 50% of the normal animals (potency ratio: 5·3) and that there was no significant difference in the resistance acquired by the mice due to vaccination with strain 6651 as against that acquired by the mice due to vaccination with strain G 17 M. An experiment carried out to ascertain the best route for the administration of the immunizing doses of killed yeast-phase suspensions yielded no significant differences in resistance achieved through immunization by any of the different routes when the mice were challenged with graded doses of strain G 17 M except in the case of those mice which were immunized by the oral route and these did not exhibit greater resistance than the controls.

Finally, the effect of prior infection on subsequent challenge was investigated. In this experiment groups of mice were inoculated intravenously with a yeast-phase suspension of strain 6651 which had been shown to produce sublethal infection. Some 90 days later all these mice were challenged intravenously with varying amounts of strain G 17 M organisms. Results show that these mice were significantly more resistant to infection by the challenging doses of strain G 17 M than were normal mice, but that this resistance was no greater than in the case of mice which had previously been immunized with killed suspensions of strain 6651.

The authors therefore infer from these results that there is no advantage in using either method in preference to the other, and that consequently such

information may be significant in the development of non-viable vaccines designed to replace viable vaccines which, in some cases, carry a potential danger.

C. J. La Touche

RICKETTSIAE

HOPPS, Hope E., JACKSON, Elizabeth B., DANAUSKAS, J. X. & SMADEL, J. E. **Study on the Growth of Rickettsiae. III. Influence of Extracellular Environment on the Growth of** *Rickettsia tsutsugamushi* **in Tissue Culture Cells.** *J. Immunology.* 1959, Feb., v. 82, No. 2, 161–71, 3 figs. [45 refs.] **IV. Effect of Chloramphenicol and Several Metabolic Inhibitors on the Multiplication of** *Rickettsia tsutsugamushi* **in Tissue Culture Cells.** *Ibid.*, 172–81, 1 fig. [29 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 814.]

SHAPIRO, M. I. **Experimental Study of Strains of Tick-Borne Rickettsias isolated on One of the Islands off the South Coast.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 10, 1664–71, 3 figs. [12 refs.] [Translated from Russian.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1017.]

BOOL, P. H. **Studies on** *Ehrlichia canis* **(syn.** *Rickettsia canis***).** *Acta Tropica.* Basle. 1959, v. 16, No. 2, 97–107, 7 figs. (5 coloured on pl.) [34 refs.]

BACTERIOPHAGES

PRÉVOT, A. R. & THOUVENOT, H. Nouvelles recherches sur le bactériophage 1452 actif sur les *Corynebacterium anaérobies.* [**Further Studies on Phage 1452 Active on Anaerobic Corynebacteria**] *Ann. Inst. Pasteur.* 1959, Aug., v. 97, No. 2, 234–6.

The English summary appended to the paper is as follows:—

"The experiments show that phage 1452 behaves towards anaerobic Corynebacteria like any phage towards its sensitive genus. This comportment reveals a close relationship between the various species of Corynebacteria as already evidenced by serological studies.

"Phage lysis confirms the antigenic relationships and differences of the various species.

"But above all, phage 1452 allows the diagnosis of the genus, since the phage is inactive towards related genera, which might be mistaken for *Corynebacterium Ramibacterium, Propionibacterium, Bifidibacterium, Actinobacterium.*"

FREDERICQ, P. Transduction par bactériophage des propriétés colicinogènes chez *Salmonella typhi-murium.* [**Bacteriophage Transduction of Colicinogenic Properties in** *Salm. typhi-murium*] *C.R. Soc. Biol.* 1959, v. 153, No. 2, 357–60.

In previous studies (*Ann. Review Microbiol.*, 1957, v. 11, 7) on recombination between bacterial strains one of which was colicinogenic, the genetic factor determining the production of colicine behaved as if it were independent of the bacterial chromosome. Since it is generally believed that characters transduced by bacteriophages always form part of the bacterial chromosome, experiments were done to see if the colicinogenic property can be transduced.

It was found that transduction of the markers controlling the ability to use histidine and tryptophan by phage PL 22 grown in a prototrophic strain of *Salmonella typhi-murium* LT 2 to a histidine- and tryptophan-requiring mutant occurred with the same frequency, whether or not either strain was colicinogenic. The transduced cells formed the colicine specific to the receptor cells and no evidence of transduction of the ability to form colicine was obtained.

The following selective technique was evolved: the transducing phage and receptor strain were mixed to allow infection, were plated and then covered with a sterile layer of molten agar. 2 days later an indicator strain sensitive to the colicine was spread over the surface of the plate. Zones of inhibition were seen wherever the deep colonies produced colicine. In this way, transduction of the markers controlling the production of colicines E (2) or E (2) and I was demonstrated. Only colicinogenesis was transduced: the other markers of the transduced cell were those of the recipient. Transduction of colicinogenesis occurred in the same conditions and with the same frequency as that of other markers.

Thus, it appears that the genetic material governing the production of colicines exists in 2 states, as suggested by ALFOLDI *et al.* (*C.R. Acad. Sci.*, 1958, v. 246, 3531). In recombination it is independent of the bacterial chromosome, *i.e.*, it acts as an episome (JACOB & WOLLMAN, *C.R. Acad. Sci.*, 1958, v. 247, 154) and in transduction it forms part of the bacterial chromosome.

Janice Taverne

KOHN, A. & HERTMAN, I. **A New Type of Lysis from Without.** *Proc. Soc. Exper. Biol. & Med.* 1959, June, v. 101, No. 2, 372–4, 1 fig. [13 refs.]

When *Escherichia coli* cells which were growing exponentially were frozen and thawed, some lysed, 30–60% were no longer viable and 1–2 hours elapsed before the survivors resumed growing. Cells which had been infected with phage before freezing (phages T2, T3, T4 and T7 were used) lysed upon thawing, and there was no phage multiplication. Cells infected immediately after freezing and thawing lysed at once, again without any latent period. Multiplicities of infection were varied from 1 to 15. In a solution of 0·3M sucrose containing phage, thawed bacteria formed spheroplasts.

It is widely believed that lysis from without caused by the adsorption of a large number of phage particles

to one cell occurs because the numerous holes in the cell wall made by an enzyme from the phage tail are not sealed quickly enough [this *Bulletin*, 1955, v. 30, 432]. Similarly, the authors suggest that when bacteria are dormant after being frozen the damage done to the cell wall by the phage enzyme is not repaired and the bacteria lyse. *Janice Taverne*

LOVELESS, A. & STOCK, Jocelyn C. **The Influence of Radiomimetic Substances on Deoxyribonucleic Acid Synthesis and Function studied in *Escherichia coli* Phage Systems. I. The Nature of the Inactivation of T2 Phage *in vitro* by certain Alkylating Agents.** *Proc. Roy. Soc.* Ser. B. 1959, Apr. 21, v. 150, No. 940, 423–45, 18 figs. [19 refs.]

The effect of di (2-chloroethyl) methylamine (HN 2) on free phage T2 was studied. Phage inactivation was found to continue after the agent had been diluted out. Adsorption of phage to bacteria before plating, or addition of thiosulphate to treated phage, prevented some of the decay occurring after dilution. (HN 2 does not interfere with adsorption.) A comparison of phage survival curves obtained after treatment with the bi-functional alkylating agent HN 2 and with mono-functional agents, followed by removal of the agents by dilution or by thiosulphate, was done. It indicated that those particles whose inactivation by HN 2 could be prevented had undergone alkylation by one "arm" of the bi-functional agent only, and that their inactivation was prevented when the other "arm" was neutralized.

For mono-functional compounds, phage inactivation continuing after removal of the agent was caused by a dose-dependent, acid-catalysed breakdown of the alkylated particles.

Dose/survival curves plotted for both sorts of agents, when reaction went to completion, were shown to be exponential, and thus similar to those obtained with radiations.

It is believed that the point of attack of alkylating agents is DNA. As HN 2 does not prevent adsorption of T2, it must inactivate by interfering with a process happening later in the phage multiplication cycle, either by preventing injection of DNA or its normal synthesis. Calf thymus DNA was found to protect phage from the action of HN 2, as did polymethacrylate and sodium thiosulphate. *Janice Taverne*

HEICKEN, K. & SPICHER, G. Über die Kinetik der Inaktivierung und Reaktivierung von Phagen. II. Mitteilung. [**Kinetics of the Inactivation and Reactivation of Phages**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 1/2, 11–26, 10 figs.

In a study of the inactivation of phages by 0·06% formaldehyde it was found that the T1, T3, T5 and T7 phages and 2 staphylococcal phages were inactivated at a constant rate, which was greatest in T3 and least in T1. The rate constant of inactivation was increased 2·5-fold by doubling the concentration of formaldehyde; the temperature coefficient was 3·1, and the energy of activation was thus 19,900 calories per mole. Inactivation of the T2, T4 and T6 phages proceeded differently, with an initial rapid phase followed by a slow phase; this was considered to be due to the presence of a small proportion of phage particles which reacted slowly with formaldehyde, and it was further shown that these were not mutants. All the phages could be reactivated by treatment with histidine, and data on the kinetics of the process are presented.

[For Part I, see this *Bulletin*, 1957, v. 32, 608.]

D. J. Bauer

HEICKEN, K. & SPICHER, G. Über die Kinetik der Inaktivierung und Reaktivierung von Phagen. IV. Mitteilung. Über den chemischen Mechanismus der Formaldehydinaktivierung von Phagen. [**The Kinetics of the Inactivation and Reactivation of Phages. 4th Communication: The Chemical Mechanism of the Formaldehyde Inactivation of Phages**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 5/6, 321–32, 1 fig. [24 refs.]

A study has been made of the kinetics of the inactivation of the odd-numbered T phages by formaldehyde with the object of identifying the functional groups which are involved in the reaction. Separate determinations of the inactivation rate constant were made at various *p*H values between 5 and 10. The rate constants remained unchanged between *p*H 5 and *p*H 7 and then increased rapidly up to *p*H 10; the values for T3 and T7 phages were higher than the constants for T1 and T5 phages. The results indicated that the group reacting with formaldehyde was the same in all the phages and that it had a *p*K value of around 9·8. It could therefore be identified with some probability as the terminal amino-group of the lysine residues (*p*K 10·0). With T1 phage there was also some evidence that an acid amide group was involved in the reaction with formaldehyde. *D. J. Bauer*

KULANGARA, A. C. & SELLERS, Margret I. **Passage of Bacteriophages from Mother to Foetus in the Rat.** *Proc. Soc. Exper. Biol. & Med.* 1959, June, v. 101, No. 2, 207–11. [11 refs.]

Since antibodies are known to pass from mother to foetus across the placental barrier, the authors were interested to discover whether or not particles larger than protein molecules would also do so. Pregnant rats were inoculated by various routes with phages T3 and T1 and with 2 mycobacteriophages, and the foetuses were later removed with intact foetal membranes. The membranes and the outsides of the foetuses were washed in saline and in alcohol to reduce the chances of recovering phage from contaminating maternal blood. Foetal blood was inoculated into broth containing bacteria sensitive to the phage used, and the culture was later spotted on to indicator plates which were examined for plaques. No quantitative experiments were done.

Phage injected into the mother intravenously was never detected in the foetus. When phage was injected into the uterine lumen, however, passage to the foetus was demonstrated in 74% of the samples with T phages, and in 33% of those with mycobacteriophages. In these experiments therefore phage was only detected in

the foetus when high concentrations had been present in the uterine cavity. The biggest phage tested, D 32, had a head diameter of 80 mμ. It appears then that in certain conditions particles of this size can pass undegraded across the placental barrier.

Janice Taverne

ADAMS, M. H., **Bacteriophages.**

This book was reviewed on p. 968.

VIRUSES

In this section the abstracts are arranged as far as possible in the following order: General; Psittacosis-lymphogranuloma viruses; Pox viruses; Respiratory and other viruses; Enteric viruses; Arthropod-borne viruses; others.

GALE, C., POMEROY, B. S. & SANGER, V. L. **Characterization in Mice of a Turkey Ornithosis Virus of Low Virulence.** *J. Infect. Dis.* 1959, May–June, v. 104, No. 3, 295–9, 7 figs. [18 refs.]

This paper describes a strain of virus belonging to the psittacosis-LGV group isolated from apparently healthy turkeys which were being screened for air sac and sinus infection. It was obtained by the inoculation of mice for which animals it proved to be of very low virulence. Avirulent turkey strains have been observed by previous workers. *S. P. Bedson*

SĂRĂTEANU, D., DRĂGĂNESCU, N., PORTOCALĂ, R. & IONESCU, N. I. Pneumonia neorickettsiană. Izolarea si identificarea agentului patogen. [**Neorickettsial Pneumonitis. Isolation and Identification of the Pathogenic Agent**] *Microbiol., Parazitol., Epidemiol.* Bucharest. 1958, Nov.–Dec., v. 3, No. 6, 529–33, 4 figs.

By successive yolk sac passage an infective agent producing elementary bodies 200–500 mμ in size resembling psittacosis in appearance was isolated from the sputum of a patient suffering from primary atypical pneumonia. The agent could be adapted to mice by intranasal inoculation. In cross-agglutination tests with rabbit immune sera the agent was found to be related to the organism described by GIROUD under the name *Neorickettsia* [this *Bulletin*, 1955, v. 30, 230]. The patient's serum gave cross-fixation with psittacosis-ornithosis group antigen and agglutinated the Giroud agent to a titre of 20. *D. J. Bauer*

SARKAR, J. K., NEOGY, K. N. & LAHIRI, D. C. **Behaviour of Variola and Vaccinia Viruses in Mice.** *J. Indian Med. Ass.* 1959, Apr. 1, v. 32, No. 7, 279–81.

Freshly isolated vaccinia virus (from lymph) and variola virus were inoculated into adult and baby mice by intraperitoneal and intracerebral routes. In adult mice, no pathological changes were induced by intraperitoneal injection of either vaccinia or variola viruses. Baby mice injected by this route with variola virus developed ascites which was purulent in the late stages. All the animals were dead by the 13th post-inoculation day and the peritoneal fluid contained virus. Vaccinia virus by this route killed baby mice within 4 days.

Serial intracerebral inoculation of baby mice with vaccinia virus killed them within 6 days. During the serial passage of variola virus by this route, mice were killed by the virus in the first 2 passages. Third and fourth passage mice did not die. When killed as long as 62 days after inoculation, virus was found in their brains. In fifth and subsequent passages, mice again died but the average time to death appears to have been very much longer than that in mice inoculated with vaccinia virus. *Colin Kaplan*

TAGAYA, I. & ODA, M. **Growth of Vaccinia Virus in HeLa Cells with special reference to the Production of Soluble Antigens.** *Japanese J. Med. Sci. & Biol.* 1958, Dec., v. 11, No. 6, 483–99, 9 figs. [16 refs.]

The general picture of vaccinia virus increase in HeLa cell cultures is similar to the picture in chick chorioallantois [BRIODY and STANNARD, this *Bulletin*, 1953, v. 28, 71; MAITLAND and TOBIN, *ibid.*, 1956, v. 31, 870]. The earliest detectable rise in infectivity occurred about 10 or 11 hours after the cultures were washed to remove as much as possible of the unadsorbed virus. Haemagglutinin was first found rather later than this. Complement-fixing (CF) antigen was found in the cells 6–17 hours after infection, depending on the dose of virus inoculated. CF antigen was found earlier than this in the culture medium, but the authors are not satisfied that this is not related to residual inoculum rather than new virus. The authors confirm the findings of other workers that less than 10% of the virus is in the culture medium: 90% or more is associated with the cells even when cytopathic change is advanced. There was no difference in virus production whether HeLa cells were incubated at 30°C. or 37°C. after infection. Below 25°C., however, virus titres were greatly reduced.

Colin Kaplan

DRIESSEN, J. H. & GREENHAM, L. W. **Haemadsorption in Vaccinia-Infected Tube Tissue Cultures.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 1, 45–55, 5 figs.

The authors of this paper have shown that fowl erythrocytes will adsorb to vaccinia-infected tissue culture cells. This haemadsorption reaction appears to be specific and is inhibited by antivaccinial antibody. Erythrocytes from rabbits, mice, guineapigs, calves, sheep and men gave negative tests. All 46 fowl erythrocyte samples tested were effectively adsorbed, although only 21 of the samples were agglutinable *in vitro* by vaccinia haemagglutinin. This suggests that haemadsorption may be due to a different factor from that responsible for haemagglutination. Antisera

were investigated by inhibition of haemadsorption and by inhibition of pock formation on the chick embryo chorioallantois. The haemadsorption test was less sensitive than the pock inhibition test, and not satisfactory for antibody titrations. *Colin Kaplan*

Brown, A., Mayyasi, S. A. & Officer, J. E. **The "Toxic" Activity of Vaccinia Virus in Tissue Culture.** *J. Infect. Dis.* 1959, Mar.–Apr., v. 104, No. 2, 193–202, 2 figs. [27 refs.]

Using a mouse-brain-adapted strain of vaccinia virus subsequently passed twice in chick embryo chorioallantoic membrane, the authors have shown that large doses of virus (*e.g.* 10^7 mouse LD50) induce intense cytopathic changes in cultures of foetal mouse lung cells within 8 hours. This effect was not influenced by the presence of normal rabbit serum, but was inhibited by antivaccinial rabbit serum. By using chemical inhibitors of virus replication which were not virucidal, the authors satisfied themselves that the toxic cytopathic effect was independent of virus multiplication. They also demonstrated this point by experiments involving exposure of cells to large doses of virus (10^7 LD50) and subsequently washing out excess virus. The maximum increase of virus noted in 4 days was 4-fold, compared with a 3,000-fold increase in cultures infected with 10^4 LD50 of virus. [The findings of this group accord with those of Nishmi and Bernkopf, this *Bulletin*, 1959, v. 34, 584.] *Colin Kaplan*

Wildy, P., Stoker, M. G. P. & Ross, R. W. **Release of Herpes Virus from Solitary HeLa Cells.** *J. General Microbiol.* 1959, Feb., v. 20, No. 1, 105–12, 1 fig.

HeLa cells were infected with the HFEM strain of herpes virus in a multiplicity of 16–79 pock-forming units per cell, and after washing to remove unattached virus the cells were dispersed and isolated in droplets of medium each containing a single cell. The droplets were then assayed for virus content by inoculation on to the chorioallantoic membrane after incubation for 28–35 hours. Under these conditions 19–35% of the cells liberated virus, with an average yield of 13 pock units per cell.

In similar experiments in which the droplets were sampled at intervals virus could still be detected at the 10th hour but had disappeared at the 16th hour, and probably represented a residue of the original inoculum. New virus was detected at the 26th hour and the amount increased up to the 33rd hour, suggesting that the virus was released gradually.

[See also this *Bulletin*, 1959, v. 34, 175.]

D. J. Bauer

Black, F. L. **Growth and Stability of Measles Virus.** *Virology.* New York. 1959, Feb., v. 7, No. 2, 184–92, 4 figs. [15 refs.]

Hep-2 cell cultures in Eagle medium were infected with the Edmonston strain of measles virus in a multiplicity of 1·5 and the subsequent course of virus production was followed by plaque counts carried out on supernatant fluid removed at intervals after infection, the residue of the infecting dose having been removed by washing. Virus first appeared after 26 hours and reached a maximum titre of 10^4 after 47 hours. In cultures disrupted by freezing and thawing virus was detected after 18 hours and attained titres of 10^5–10^6. Complement-fixing antigen appeared in the cells after 24 hours and in the culture fluid after 72 hours. In a study of the rate of inactivation of the virus in culture fluid the half-life at 37°C. was found to be 2 hours. The virus was completely inactivated by exposure to *p*H values below 4·4 for 3 hours at 0°C., but was relatively stable between *p*H6 and *p*H9. The comparatively low titres attained in tissue culture fluid are evidently due to the loss of much of the virus by continuous thermal inactivation. *D. J. Bauer*

Soule, D. W., Marinetti, G. V. & Morgan, H. R. **Studies of the Hemolysis of Red Blood Cells by Mumps Virus. IV. Quantitative Study of Changes in Red Blood Cell Lipides and of Virus Lipides.** *J. Exper. Med.* 1959, July 1, v. 110, No. 1, 93–102, 1 fig. [17 refs.]

"Hemolysis of chicken red blood cells by mumps virus is associated with the release of sphingomyelin from the stromal lipoprotein and the destruction of 65 per cent of the sphingomyelin of the red cell stroma. However, the virus had no effect on isolated phosphatides extracted from the erythrocytes. The hemolytic action of the virus and changes in sphingomyelin content of the erythrocytes fail to occur at a pH of 6.0. The viral hemolysis of human erythrocytes is not associated with similar alterations in their content of sphingomyelin. The absence of lecithin from sheep erythrocytes, which are also lysed by mumps virus, is additional evidence that a viral lecithinase is not associated with the hemolytic property of mumps virus.

"Mumps virus concentrated from the amniotic fluid of viral infected chick embryos contains about 7 per cent phosphatide, 60 per cent of which is sphingomyelin."

Möbest, H. & Tolki, U. Über das Vorkommen komplementbindender, praeformierter Antikörper in normalen Kaninchenseren. [**The Occurrence of Preformed Complement Fixing Antibodies in Normal Sera of Rabbits**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 5/6, 472–8.

This paper draws attention to complement fixation given by sera of some normal rabbits with commercial mumps and psittacosis antigens. Of 19 rabbits examined 15 fixed complement with the mumps antigen and 15 with the psittacosis antigen; 12 fixed with both. The reactions were sometimes complete with serum dilutions as high as 1 in 16. The antigens were prepared from virus grown in the chick embryo—allantois in the case of mumps and yolk sac in the case of psittacosis. The injection of the allantoic fluid or a suspension of chorio-allantoic membrane from normal chick embryos produced rises in titre. *S. P. Bedson*

FROMMHAGEN, L. H. & KNIGHT, C. A. **Column Purification of Influenza Virus.** *Virology.* New York. 1959, June, v. 8, No. 2, 198–208, 4 figs. [16 refs.]

2 methods used for the purification of influenza viruses, namely chromatography on aluminium phosphate columns and red cell adsorption and elution, were compared. The following advantages of the first over the second methods were demonstrated: (1) it is more rapid and convenient; (2) it gives higher recoveries of haemagglutinating activity and yields purified materials with higher infectivity and haemagglutinating titres; (3) it avoids high temperatures of elution; (4) it avoids contamination with organic materials; (5) it yields, apart from virus particles, a non-infectious, non-haemagglutinating sedimentable material similar in many ways to sedimentable material present in normal allantoic fluid. *H. G. Pereira*

FROMMHAGEN, L. H., KNIGHT, C. A. & FREEMAN, N. K. **The Ribonucleic Acid, Lipid, and Polysaccharide Constituents of Influenza Virus Preparations.** *Virology.* New York. 1959, June, v. 8, No. 2, 176–97, 5 figs. [21 refs.]

Chemical analysis of influenza A (PR8 and DSP) and B (Lee) was studied with virus preparations purified by chromatography on aluminium phosphate columns or by red cell adsorption and elution. The concentration of lipids, polysaccharides, ribose and ribonucleic acid in comparable materials from infected and uninfected eggs was determined by chromatographic methods and by infra-red spectroscopy. Lipid content of materials from infected or uninfected eggs was essentially identical. A total lipid concentration of 18·5 ± 1·5% was estimated in terms of percentage of the dried virus or other materials. No esterified sterol could be detected in any of the preparations. The concentration of unesterified cholesterol was 6·5 ± 0·6%. Phospholipids in a total concentration of 11·5 ± 1% were fractionated by silicic acid chromatography and analysed by infra-red spectroscopy which revealed the presence of cephalin (49%), sphingomyelin (36%) and lecithin (15%). A glycolipid making up 5% of the total compound lipids was also detected. Polysaccharide concentration of viral or control materials varied between 4% and 6% and the same proportions of galactose, mannose, fucose and amino sugar was found in both types of materials. Total RNA concentration expressed as percentage of dried preparations gave values ranging from 0·69% to 0·81% for virus materials and from 0·12% to 0·25% for non-infectious materials. *H. G. Pereira*

BORECKÝ, L., with the technical assistance of L. MAASOVÁ & I. KIANICKOVÁ. **A Factor destroying Virus Receptors in Pneumococcal Cultures. II. The Effect of "Pneumococcal Factor 103" on Erythrocyte Receptors and Inhibitors.** *Acta Virologica.* Prague. 1958, Oct.–Dec., v. 2, No. 4, 201–7. [12 refs.]

The author has previously shown [this *Bulletin*, 1959, v. 34, 292] that filtrates of a culture of pneumococci possess receptor-destroying activity, and in the present work this effect has been studied in greater detail. The receptors of chick red cells for mumps, Newcastle disease and PR8 viruses were destroyed by incubation with the pneumococcal factor for 1½ hours at 37°C., but the receptors for Lee, influenza C and swine influenza viruses were more resistant. A similar effect was observed with guineapig and ground squirrel red cells, and the results indicated that the pneumococcal factor destroyed virus receptors in accordance with the receptor gradient. The pneumococcal factor further resembled the receptor-destroying enzyme of *Vibrio comma* in possessing the ability to destroy egg white and serum inhibitors, and was particularly active against the inhibitor of influenza C virus present in normal rat serum. *D. J. Bauer*

VOLÁKOVÁ, N. & JANDÁSEK, L. **A Thermostable Inhibitor of Newly Isolated Influenza Virus Strains in Guinea Pig Serum.** (Preliminary Report.) *Acta Virologica.* Prague. 1959, Apr., v. 3, No. 2, 109–12. [10 refs.]

The haemagglutinating activity of some strains of Asian influenza virus was found to be inhibited by normal guineapig sera. The inhibitor resisted boiling for at least 20 minutes. Normal guineapig serum heated at 56°C. for 30 minutes was also shown to neutralize the infectivity of some virus strains. Haemagglutination-inhibition by normal guineapig serum was not observed with influenza virus strains other than Asian. Different strains of Asian virus varied in sensitivity to this inhibitor and inhibition of haemagglutination and of infectivity were not correlated. Infection of fertile eggs by one strain of Asian influenza virus was prevented by normal guineapig serum injected up to 4 days before the virus inoculum.

A similar inhibitor was found in cow serum but not in rabbit, mouse, horse, pig, rat or sheep sera.
H. G. Pereira

HENNEBERG, G. & LANGE, F. C. Über die toxische und antigene Wirksamkeit von Viren. I. Mitteilung: Quantitative und zeitliche Bedingungen für die toxische Wirksamkeit von Influenzaviren. [**The Toxic and Antigenic Activity of Viruses. Quantitative and Temporal Conditions for the Toxic Action of Influenza Viruses**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 1/2, 26–40. [26 refs.]

In an investigation of the toxicity of the PR8 strain of influenza virus in guineapigs death could be produced by the daily intraperitoneal injection of virus provided that the dose exceeded a certain minimum. In similar experiments in which the A/Singapore 1/57 strain was injected for periods ranging up to 30 days 75% of the animals died. The mean survival time was also significantly reduced as the dose of virus was increased. The mortality from the toxic effect of the virus could be reduced to 16·7% by previous immunization with depot vaccine, and to 8·3% by previous exposure to the toxin. The PR8 strain was considerably more toxic than the A/Singapore 1/57 strain.
D. J. Bauer

COLOBERT, L., DUFFRENE, A. & FONTANGES, R. Une nouvelle méthode photométrique de titrage du pouvoir hémagglutinant des mixovirus. I. Virus grippal type B. [**A New Photometric Method of Estimating the Haemagglutinating Activity of Myxoviruses. I. Influenza virus B**] *C.R. Soc. Biol.* 1959, v. 153, No. 3, 428–31, 2 figs.

The rate of sedimentation of human erythrocytes treated by influenza B virus particles or ether-extracted haemagglutinin [this *Bulletin*, 1956, v. 31, 1046] was studied by photometry. A method for the estimation of haemagglutinating activity was developed with basis on the exponential relation between red-cell sedimentation rate and haemagglutinin concentration.

H. G. Pereira

COLOBERT, L. & DUFFRENE, A. Propriétés basiques de l'hémagglutinine du virus grippal "B". [**Basic Properties of Influenza B Virus Haemagglutinin**] *C.R. Soc. Biol.* 1959, v. 153, No. 3, 431–3.

Hemagglutinin prepared by ether treatment of influenza B virus was submitted to chromatography on Amberlite XE-64 columns. Haemagglutinating activity was completely retained in columns equilibrated with M/15 buffers, at *p*H 6·5 or lower. Elution by perfusion with buffers of increasing *p*H gave a wide band of fractions with low haemagglutinating titres.

It is suggested that the haemagglutinin is a basic protein which may play a role analogous to that of protamines or histones described in other viruses.

H. G. Pereira

WESSLÉN, T., HERMODSSON, S. & PHILIPSON, L. **Interference between Influenza and Poliomyelitis Viruses in Tissue Culture.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 1, 31–44, 4 figs. [31 refs.]

The capacity of influenza virus to interfere with the multiplication and cytopathic action of poliovirus was studied in cultures of monkey kidney tissue. An Asian strain of influenza virus was used in most experiments and shown to multiply, reaching high infectivity titres with minimal cytopathic effect in monkey kidney cultures.

Evidence suggesting that surviving cells were actively supporting influenza virus multiplication was obtained by means of the haemadsorption technique. Surviving cells in influenza-infected cultures were protected against the cytopathic action of poliovirus. The degree of interference and the time required for it to be established varied with size of interfering and challenge doses. The yield of poliovirus by monkey kidney cells was also shown to be depressed by previous infection with influenza virus. A period of 12 hours between inoculations of interfering and challenge viruses was required for this effect to be demonstrated. Influenza virus inactivated by heat or ultra-violet light had no interfering activity.

Evidence is presented suggesting that interference is not due to impairment of adsorption of the challenge virus. *H. G. Pereira*

LANGE, F. C. Über den Einfluss der geweblichen Organisation auf die Wirksamkeit des Adsorbens in einem Depot-Impfstoff. [**The Influence of Tissue Repair on the Effectivity of the Adsorbent Medium in Depot Vaccines**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 3/4, 198–211, 1 fig. [13 refs.]

An investigation has been made of the effect of the tissue response upon the adsorbent power of aluminium oxide used in depot vaccines. Mice were inoculated subcutaneously with 0·5–0·75 gm. of gamma aluminium oxide in order to form depots; after 3 days the material was removed, and it was found that the adsorption of the PR8 strain of influenza virus by the material still obeyed the Freundlich adsorption isotherm. In further experiments it was shown that depots of gamma aluminium oxide could take up small amounts of virus when viraemia was produced artificially by inoculating the mice intravenously or intraperitoneally with PR8 virus. *D. J. Bauer*

COOK, M. Katherine, ANDREWS, B. E., FOX, H. H., TURNER, H. C., JAMES, W. D. & CHANOCK, R. M. **Antigenic Relationships among the "Newer" Myxoviruses (Parainfluenza).** *Amer. J. Hyg.* 1959, May, v. 69, No. 3, 250–64. [31 refs.]

Antigenic relationships among members of the Myxovirus group were studied by means of complement-fixation, virus neutralization and haemagglutination-inhibition tests. The viruses investigated included influenza A, B and C, Sendai, haemadsorption (HA) viruses types 1 and 2, croup-associated (CA) virus, mumps and Newcastle disease (NDV). No antigenic relation could be demonstrated between influenza A, B or C and the remaining Myxoviruses included in this study. Complement-fixation tests performed with pooled guineapig antisera failed to show cross reactions, except in the case of Sendai and HA_2 viruses. Cross-reactions between these 2 viruses were not entirely reciprocal, and were particularly marked in tests performed with Sendai antiserum suggesting that an antigen common to these 2 viruses is present in higher concentration in Sendai than in HA_2 virus. An antigenic relationship between Sendai and HA_2 virus was also demonstrated, but to a lower extent, by complement-fixation tests with viral antigens, by haemagglutination-inhibition and by serum neutralization. Sendai and HA_2 viruses are considered to be sub-types of the same virus type. Low levels of cross reactions between Sendai, mumps, CA, HA and NDV were revealed in complement-fixation tests done with antisera from individual guineapigs or with human convalescent sera.

The present findings support the recently proposed classification of Myxoviruses [ANDREWES *et al.*, this *Bulletin*, 1959, v. 34, 1056] in which the new members of the group are gathered under the name *Myxovirus parainfluenzae* with 3 subgroups consisting of *M. parainfluenzae 1* (Sendai and HA_2), *M. parainfluenzae 2* (CA) and *M. parainfluenzae 3* (HA_1). *H. G. Pereira*

PEREIRA, Marguerite S., PEREIRA, H. G. & ALLISON, A. C. **Use of Gel Diffusion Precipitation Test in the Diagnosis of Adenovirus Infections.** *Lancet.* 1959, Mar. 14, 551–2, 1 fig. [12 refs.]

The gel diffusion precipitation test has been adapted to the detection of antibody to adenoviruses in human sera. Type 5 adenovirus antigen obtained from HeLa cell cultures and purified by fluorocarbon treatment was placed in the centre well of an agar plate, and rabbit specific antiserum, acute- and convalescent-phase sera from patients suffering from type 5 and type 3 adenovirus infection, and rabbit antiserum to HeLa cells were placed individually in the 6 peripheral wells. The plate was then left at room temperature for 2 days, and continuous lines of precipitate developed between the antigen and the sera containing type 5 antibody; the specificity of the method was indicated by the absence of precipitate with the remaining sera. In a comparison of the method with the complement-fixation test carried out on 177 miscellaneous human sera the precipitation test generally gave a positive result when the complement-fixation titre exceeded 80. A result of diagnostic value was obtained by the precipitation test with 24 of 26 paired sera from patients suffering from adenovirus infections of types 3, 5, 7 and 14 in 11 of whom the diagnosis had been established by isolation of the virus. *D. J. Bauer*

ROSENBAUM, M. J., FRIEDMAN, M. & LIEBERMAN, M. **A Comparison of Two Sampling Methods for the Isolation of Adenovirus.** *J. Lab. & Clin. Med.* 1959, June, v. 53, No. 6, 966–9, 1 fig. [10 refs.]

Attempts to isolate adenoviruses from throat washings and throat swabs collected from 96 U.S. Navy recruits gave 36 (38%) positive results. No significant difference was found between the numbers of adenoviruses isolated by each of the 2 sampling methods. The total number of isolations was, however, higher when the results of the 2 methods were combined.
H. G. Pereira

NÁSZ, I. & TÓTH, M. **Cytomorphological Changes in Human Embryonic Kidney Tissue Cultures infected with Adenovirus Type 5 Strains.** *Acta Microbiologica.* Budapest. 1959, v. 6, No. 1, 85–92, 1 text fig. & 13 figs. on 2 pls. [14 refs.]

Cytopathic changes associated with multiplication of adenovirus type 5 in embryonic human kidney cultures are described. The earliest changes were observed 16 to 30 hours after inoculation and consisted of the formation of intranuclear eosinophilic material arranged either diffusely or forming round or oval aggregates often surrounded by a clear zone and a granular outer ring. From 30 to 45 hours the eosinophilic granules appeared to form clusters which subsequently gathered in the centre of the nucleus. At later stages the central intranuclear mass tended to become basophilic and was surrounded by a hyaline zone. The cytoplasmic area at this stage was reduced and the cells were rounded and tended to detach from the glass. Some cells showed different changes consisting of the formation of intranuclear eosinophilic bodies surrounded by basophilic material or rod-shaped crystal-like bodies. The various stages of cytopathic changes occurred asynchronously in the course of infection. *H. G. Pereira*

NÁSZ, I. & TÓTH, M. **Adenovirus in Human Embryonic Kidney Cells.** [Correspondence.] *Lancet.* 1959, Aug. 15, 128, 6 figs.

A description of cytopathogenic changes.

UCHIDA, S., HOSHIKA, T., YAMAMOTO, H., KOIKE, K., KOSEKI, S. & FURUNO, A. **Relationships between Types of Adenovirus indicated by Heterologous Neutralization.** *Japanese J. Exper. Med.* 1959, Apr., v. 29, No. 2, 121–9, 1 fig. [12 refs.]

"Type-specific rabbit antiserums against Adenovirus Types 1 to 14 except Type 12 were studied by cross neutralization test. Prior to this study the conditions necessary to obtain highly reproducible results were investigated.

"Homologous antibody titers of most of these serums were 1 : 28 to 1 : 1024.

"Although the heterologous neutralizations were found only rarely and their titers were usually low, the existence of antigenic relationships between Types 7, 11 and 14, between Types 3 and 7 and between Types 8 and 9 were recognized."

PRICE, W. H., EMERSON, Hope, IBLER, Irene, LACHAINE, R. & TERRELL, A. **Studies of the JH and 2060 Viruses and their Relationship to Mild Upper Respiratory Disease in Humans.** *Amer. J. Hyg.* 1959, May, v. 69, No. 3, 224–49. [22 refs.]

The role played by virus JH [PRICE, W. H., this *Bulletin*, 1958, v. 33, 621] and virus 2060 [PELON *et al.*, *ibid.*, 1957, v. 32, 629] in the aetiology of upper respiratory infections was investigated by laboratory, clinical and epidemiological methods. Virus isolation from nasopharyngeal secretions of patients with upper respiratory infections was attempted with monkey kidney tissue cultures. Results were often negative even when evidence of infection by JH or 2060 viruses could be demonstrated by serological methods. The frequency of virus isolations varied in different outbreaks and positive results were only obtained with samples collected during the first or second days of clinical symptoms. Virus concentration in most of the positive secretions was low and blind passages were often required before cytopathic effects could be detected. Serum neutralization tests carried out with rabbit antisera failed to reveal antigenic differences between JH virus strains and 2060 virus. Tests performed with human convalescent sera allowed, however, the distinction of 2 groups of strains designated JH_1 and JH_2, the latter being the more closely related to 2060 virus. Attempts to demonstrate complement-fixing and haem-agglutinating activities of JH viruses gave negative results.

JH viruses were associated with upper respiratory illnesses which would ordinarily be diagnosed as "colds". Serological tests and virus isolation studies revealed that 12% of 901 mild respiratory illnesses

observed over a period of 3 years was associated with JH or 2060 viruses. It was also shown that 50% of infections with JH and 2060 viruses were not associated with any illness. Susceptibility to infection by JH viruses was in general correlated with low serum levels of virus-neutralizing antibody. Virus-neutralizing activity was detected in nasal secretions collected during convalescence from infection by JH viruses. The factor responsible for this activity had some properties of neutralizing antibodies and its relationship to resistance to infection is discussed.

Serological surveys and epidemiological studies revealed that JH and 2060 viruses cause widespread infection in the United States but that these viruses do not spread readily under conditions existing among the family groups investigated. It is suggested that the major viruses responsible for the "-common cold" have not as yet been identified.

Vaccination with formalin-inactivated JH or 2060 viruses was followed by rises in neutralizing antibodies to both viruses. *H. G. Pereira*

PHILIPSON, L. & ROSEN, L. **Identification of a Cytopathogenic Agent called U-Virus recovered from Patients with Non-Diphtheritic Group and from Day-Nursery Children.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 1, 25–30. [14 refs.]

Three strains of U-virus [PHILIPSON and WESSLÉN, this *Bulletin*, 1958, v. 33, 801; PHILIPSON, *ibid.*, 995 *bis*, 1188] were studied by serum neutralization, complement fixation and haemagglutination-inhibition and shown to be antigenically related to ECHO-11 virus. *H. G. Pereira*

DEIBEL, R. **Plaque Formation in Monolayers of FL Cells infected with the Hemadsorption Type 1 Virus.** [Correspondence.] *Virology.* New York. 1959, June, v. 8, No. 2, 262–3, 1 fig.

RENOUX, G., NATAF, R. & GIROUD, P. La culture du virus trachomateux. [**The Cultivation of Trachoma Virus**] *Rev. Internat. du Trachome.* 1959, v. 36, No. 2, 182–90.

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1061.]

FINCH, J. T. & KLUG, A. **Structure of Poliomyelitis Virus.** *Nature.* 1959, June 20, v. 183, 1709–14, 4 figs. [25 refs.]

An X-ray diffraction study of poliovirus crystal is presented. As a result of this and previous work on tomato bushy stunt virus [CASPAR, this *Bulletin*, 1956, v. 31, 955] and turnip yellow mosaic virus (KLUG *et al.*, *Nature*, 1957, v. 179, 683 and *Biochim. Biophys. Acta*, 1957, v. 25, 242) and the suggestions of CRICK and WATSON [this *Bulletin*, 1956, v. 31, 955] a structure for the virus particle and crystal is suggested. It is thought that the virus particle consists of 60 sub-units each 60–65 Å units in diameter arranged as a shell with icosahedral symmetry. It is suggested that the various components observed in density gradient analysis of poliovirus preparations [LEBOUVIER *et al.*, *ibid.*, 1958, v. 33, 412] might be identified with the following structures. The D fraction is the complete virus particle, containing protein sub-units surrounding a nucleic acid core. The C fraction is probably the empty protein sub-unit shells, and the lighter fraction B is probably groups of protein sub-units as are probably poliovirus soluble antigens.

The crystal structure deduced from X-ray studies of wet crystals is different from that obtained by STEERE and SCHAFFER (*Biochim. Biophys. Acta*, 1958, v. 28, 241). These authors obtained evidence that the crystals consist of virus particles close packed in a face-centred cubic arrangement. The wet crystals appear not to be close packed, but body-centred with a distance of 304 Å from centre to centre as opposed to 273 Å found for close packed particles in electron micrographs. Each virus particle is surrounded by 8 others. Successive layers are displaced so that each particle lies nearly symmetrically over the pair below. The unit cell is orthorhombic with edge lengths $a = 353$ Å, $b = 378$ Å and $c = 320$ Å. These values closely approximate to their mean value and imply that the crystal lattice is very nearly cubic.

[The paper contains an account of the technical difficulties encountered in the study and the methods employed to overcome them.] *A. J. Beale*

ACKERMANN, W. W. **Cellular Aspects of the Cell-Virus Relationship.** *Bact. Reviews.* 1958, Dec., v. 22, No. 4, 223–39, 7 figs. [64 refs.]

The part played by the cell in the multiplication cycle of viruses is reviewed in the light of the information so far obtained with poliomyelitis and influenza viruses. Two phases can be recognized in the initiation of infection, both of which obey first-order kinetics: the rapid formation of a cell-virus complex which can be neutralized by specific antibody but from which virus cannot be extracted, and the slower formation of a system which is insusceptible to antibody. According to recent views the virus-antibody complex is irreversible and a small fraction of virus is always present which is insusceptible to neutralization.

Influenza virus becomes attached to cells by 2 types of bond, one involving a polysaccharide and blocked by *Vibrio comma* [*cholerae*] neuraminidase, and another involving potassium ions and blocked by α-amino-*p*-methoxyphenylmethanesulphonic acid, the formation of both bonds being necessary for the initiation of infection. Once within the cell the virus particle appears to disintegrate and the formation of new virus material takes place, a process which is practically independent of changes in the nutrient composition of the external medium.

Poliomyelitis virus first appears in the cytoplasm of HeLa cells 4 hours after infection and then appears to multiply exponentially; release of virus is not a sudden occurrence but is prolonged over a period of several hours, and apparently takes place by a process of transudation of the cytoplasm.

The number of virus particles formed by a single cell probably lies between 50,000 and 300,000, but sufficient ribonucleic acid is formed to account for 3 times, and protein 30 times, this number; there is also no correlation in the distributions of infectivity, new protein and new ribonucleic acid, and this last differs from the virus particles in its base composition.

These findings may be interpreted as suggesting that the presence of virus causes the cell to enter a phase of metabolic activity comparable to that preceding mitosis, during which formation of new virus occurs almost as an incidental phenomenon. *D. J. Bauer*

HOLLAND, J. J., MCLAREN, L. C. & SYVERTON, J. T. **The Mammalian Cell Virus Relationship. IV. Infection of Naturally Insusceptible Cells with Enterovirus Ribonucleic Acid.** *J. Exper. Med.* 1959, July 1, v. 110, No. 1, 65–80, 3 figs. [20 refs.]

The authors have previously demonstrated that the difference between cells susceptible and insusceptible to poliovirus is that the former contain specific virus receptors. They also showed that insusceptible as well as susceptible cells can be infected by RNA extracted with phenol from intact virus, yielding more intact virus [this *Bulletin*, 1959, v. 34, 953]. The present paper extends and confirms this work and shows that it is applicable not only to poliovirus but also to other Enteroviruses. RNA extracted from poliovirus by phenol produces infection and destruction of susceptible cells. The infectivity of the RNA is greater in hypertonic solutions (1 M NaCl) than weaker solutions (0·1 M NaCl). It also differs from intact virus in being destroyed by ribonuclease. The RNA will also infect insusceptible cells, although in these only 1 cycle of infection occurs since the newly produced virus, being indistinguishable from normal virus, is not adsorbed to the cells and hence successive cycles of infection and mass cellular degeneration do not occur. The RNA will also infect non-susceptible animals. With massive doses of virus it was found that intact virus infects non-susceptible cells but only 1 out of 10^8 particles infective for susceptible cells was effective for non-susceptible cells.

RNA preparations were not uniformly effective for all cell types; in particular human amnion cells among susceptible cells and a line of cotton tail rabbit papilloma cells (Minn. 56-8-8) among non-susceptible cells gave poor yields of poliovirus. Similar results occurred *in vivo*, thus chicks are relatively insensitive to intracerebral inoculation of RNA. Essentially similar observations have been made for other members of the Enterovirus family (Coxsackie A9, B1 and ECHO 8). The authors are careful to point out that these experiments leave open the question of whether some protein moiety is essential for the infectivity of the RNA extracted by phenol from these virus preparations. They also note that *in vivo* susceptibility may well involve other factors as well as the specific cellular receptors for virus which are of paramount importance for cells in culture. *A. J. Beale*

(3111)

DREES, O. & STUBB, Eva. Über die Infektiosität der Ultrazentrifugenkomponenten in partiell gereinigten Poliomyelitisvirus-Präparaten. [**The Infectivity of Ultracentrifuge Components of Partially Purified Poliomyelitis Virus Preparations**] *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 2, 272–81, 1 fig. [20 refs.]

The English summary appended to the paper is as follows:—

"Preparations of partially purified and concentrated poliovirus (Brunhilde and MEF$_1$ strains harvested from infected tissue cultures of trypsinized monkey kidney cells) have been found by ultracentrifugal analysis to contain two or three distinct components with sedimentation constants of 155–163 S, 83–95 S and 15–25 S respectively. The sedimentation rate of the infectivity determined by centrifugation in an improvised separation cell indicated that at least 99.9% of the infectivity was associated with the fastest sedimenting component (155–163 S)."

DREES, O. Über die Darstellung und Formaldehydinaktivierung von partiell gereinigtem und angereichertem Poliomyelitis-Virus. [**The Preparation and Formalin Inactivation of Partially Purified and Concentrated Poliomyelitis Virus**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 7/8, 489–505, 6 figs. [27 refs.]

The Brunhilde strain of poliomyelitis virus in the form of infected supernatant fluid from monkey kidney cell cultures was subjected to purification by the method of SCHWERDT and SCHAFFER [this *Bulletin*, 1957, v. 32, 906], which involves precipitation with methanol at *p*H 4 and adsorption onto kieselguhr with subsequent elution. A volume concentration of 1,000 : 1 was attained, with retention of 64% of the initial infectivity and purification of 125-fold based on total protein content. Ultracentrifugation analysis showed that the product contained 3 components with sedimentation constants of 163, 95 and 20 S in relative proportions of 50, 17 and 33%; 90% of the infectivity was found to reside in the 163 S component. Studies of the kinetics of the inactivation at 37°C. by 0·0029 M formaldehyde of both impure and purified virus showed a slight reduction in gradient of the inactivation curve after 24 hours. Inactivation was complete after 100 hours, and no infective virus could be found in inactivated material concentrated 10-fold by ultracentrifugation. *D. J. Bauer*

DE SOMER, P., DE MAEYER, E. & PRINZIE, A. Description d'un test d'antigénicité du vaccin antipoliomyélitique. [**A Method of Assaying Potency of Poliomyelitis Vaccine**] *Arch. Belges Méd. Sociale, Hyg., Méd. du Travail et Méd. Légale.* 1959, Feb., v. 17, No. 2, 119–27, 2 figs.

The authors state that the method of assaying the potency of poliovaccine proposed by the U.S. minimum requirements is very unreliable. This method involves the inoculation of groups of 12 rhesus or cynomolgus monkeys and the determination of the geometric mean

antibody response. This method provides more information about the health of the animals than the strength of the vaccine. An alternative method using 1 dose of vaccine in 1-week-old chicks is proposed which is based on the observation that there is a linear relationship between the $\log_2$ geometric mean titre and the $\log_{10}$ of the vaccine concentration. The distribution of antibody levels in individual chicks followed a normal curve and if 30 animals were used the 95% confidence limits fell within 1 $\log_2$ unit. With groups of 30 animals the slope of the line was found to be 0·74 for 14 curves. It was therefore possible to compare 2 vaccines by using a 4-point assay system. Knowing the slope of the line only 2 dilutions of unknown and reference vaccine are required to perform an assay. An example is worked out in detail. The method enables vaccines differing by 3-fold to be distinguished 95 times out of 100. *A. J. Beale*

GHENDON, I. Z. & MARCHENKO, A. T. **Use of White Rats for Testing Immunogenic Properties of Poliomyelitis Antigens.** *Acta Virologica.* Prague. 1959, Apr., v. 3, No. 2, 89–95. [11 refs.]

The authors correctly observe that the ideal system for measuring antigenic potency of polioviruses and vaccines has not yet been found. They have investigated the response of white rats. These animals (150 gm.) respond well to all 3 types of poliovirus when given 2 doses 14 days apart either intravenously or intraperitoneally and bled 7 days after the second dose. Alternatively 2 doses intravenously with 5 days between and bleeding 5 days later gave good results. 2 doses proved to be essential when either antigen extinction or geometric mean titre was used as the measure of response to antigenic stimulation. The white rats behaved in a very similar fashion to guineapigs although the responses showed less individual variation in rats. White rats are hardy, relatively standard, laboratory animals compared with guineapigs, and share with this species the advantage of being non-susceptible to living polioviruses which may therefore be assayed for potency in them. *A. J. Beale*

DREES, O. Experimentelle Beiträge zur Desinfektionsmittelprüfung bei Poliomyelitis. II. Versuche zur hygienischen Händedesinfektion. [**Experimental Contribution to the Testing of Disinfectants against Poliomyelitis. II. Experiments on the Hygienic Disinfection of the Hands**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 7/8, 539–50.

Fluid from monkey kidney tissue cultures infected with the Brunhilde, Mahoney, Lansing, MEF1, Leon or Saukett strains of poliomyelitis virus was mixed with an equal volume of disinfectant solution and left at room temperature for 2 minutes; the mixture was then diluted 1 : 50 with buffered saline and tested for infectivity in tissue cultures. A reduction of infectivity of more than 4 log units was produced by 1% chloramine, 0·1% potassium permanganate and 1% Havisol (a halogenated phenol combined with a synthetic detergent and a skin-protecting substance); the same substances in one-tenth of the above concentrations were ineffective. In similar experiments in which 10% serum was present in the mixtures inactivation was only obtained with 0·5% potassium permanganate; when cell detritus obtained from culture fluid by centrifugation was used as the infectious material 2% chloramine was ineffective; satisfactory inactivation could be obtained with 2% Havisol, and this preparation was also effective in inactivating virus deposited on the skin of the fingers.

[For Part I, see this *Bulletin*, 1957, v. 32, 362.]

D. J. Bauer

WEIGAND, H. **Interference between Coxsackie Viruses in Mice.** *Proc. Soc. Exper. Biol. & Med.* 1959, May, v. 101, No. 1, 103–6, 1 fig.

Coxsackie A14 causes paralysis in adult mice (Albany strain) when inoculated intraperitoneally or intraspinally. Prior intraperitoneal injection with other Coxsackie viruses of either group A or B (with the notable exception of Coxsackie A7) interferes with a subsequent intraperitoneal but not intracerebral dose of Coxsackie A14. The effect was more fully studied with Coxsackie A10, 21 and 1 and B1 and 5. For Coxsackie A10 and 21 the maximal effect was noted at 2 days with a second zone of interference between 4 and 6 days. Coxsackie A10 (titre $10^{-8·5}$) appeared more effective than A21 (titre $10^{-4·2}$) against a challenge dose of $10^{7·5}$ LD50 of Coxsackie A14. Unfortunately the figure showing the results obtained with prior treatment with Coxsackie B1 and 5 is inadvertently omitted. Apparently Coxsackie B1 interferes with Coxsackie A14 given at 6 days, 9–12 days and 20 days later.

A. J. Beale

ARCHETTI, I., DUBES, G. R. & WENNER, H. A. **A Comparative Study of the Prototypic Hill Strain of ECHO Virus, Type 9, and Several Coxsackie-Like Viruses Related to it Antigenically.** *Arch. f.d. gesamte Virusforschung.* 1959, v. 9, No. 1, 73–91, 4 figs. [Numerous refs.]

A comparison was made between the prototype Hill strain of ECHO 9 virus (isolated from a healthy child) and several strains of antigenically similar virus isolated from people with aseptic meningitis, a rash or both. The work is complementary to and confirmatory of a similar study by TYRRELL *et al.* [this *Bulletin*, 1958, v. 33, 803].

11 pathogenic strains from Italy, England, Canada, Denmark and the U.S.A. were studied. The pathogenic strains were antigenically more closely related to each other than to the Hill strain. They were ECHO 9 prime strains in the sense that their antisera neutralized them and the prototype strain equally well whereas serum against the prototype Hill strain was less effective against the pathogenic viruses than against the homologous virus.

It is pointed out that this does not necessarily imply a broader antigenic specificity for the pathogenic strains since some non-antigenic character affecting the kinetics

of a conventional neutralization test may equally cause the observed result. One such character which does vary from strain to strain of ECHO 9 is rate of adsorption to monkey kidney cells, the Hill strain being adsorbed more slowly than other strains. The Hill strain contains 3 plaque varieties (small, large and huge) all of which, including huge, are smaller than the plaques of the other strains studied. The Hill strain alone failed to multiply in suckling mice.

The failure of strains of ECHO 9 to produce paralysis in mice on first isolation is due to the low titre of virus. *A. J. Beale*

Cooney, M. K., Boyd, L. E. & Bauer, H. **ECHO-9 Virus Antibody Titrations in a HeLa Cell System.** *Proc. Soc. Exper. Biol. & Med.* 1959, May, v. 101, No. 1, 180–82, 1 fig.

Using an ECHO 9 virus strain adapted to grow in HeLa cells [Archetti *et al.*, this *Bulletin*, 1957, v. 32, 1200] the authors found that ECHO 9 neutralizing antibody titrations could be readily performed by using these cells. In 1957 there was an extensive outbreak of ECHO 9 meningitis in and around Minneapolis. Monkey kidney cultures were successfully used to isolate the virus but not HeLa cells. The isolation rate was 2% in patients with acute and convalescent serum neutralizing antibody levels of less than 4, and 77% in patients showing a 16-fold or greater rise in titre in convalescence. *A. J. Beale*

Rev. Serviço Especial De Saúde Pública. Rio de Janeiro. 1958, June, v. 10, No. 1, 5–183, illustrated. Simpósio sôbre Arborviroses. [**Symposium on Arborviruses**]

This symposium contains papers of local interest to Brazil (where, for instance, Venezuelan equine encephalomyelitis virus has been isolated from monkey, man, rodent and mosquito) and more general papers. It is divided into 4 sections—Laboratory diagnosis, Clinical Subjects and Pathology, Epidemiology, Control and Prevention.

The papers are in the Portuguese language, and the whole should form a useful source of information to readers of that language. *Charles Wilcocks*

Traub, E. & Schwöbel, W. Über die Leistungsfähigkeit des intracerebralen Mäusetestes und der Gewebekultur als Methoden zum Nachweis kleinster Mengen von EEE-Virus im Gewebe. [**The Detection of Small Amounts of EEE Virus. The Sensitivity of the Intracerebral Inoculation of Mice and of Tissue Cultures Respectively**] *Zent. f. Bakt.* I. Abt. Orig. 1958, v. 173, Nos. 7/8, 506–23. [19 refs.]

In a comparison of the sensitivity of mouse inoculation and tissue culture methods for the detection of virus, suspensions of various organs of mice taken at various times after subcutaneous infection with eastern equine encephalomyelitis virus were inoculated into mice intracerebrally and also used for the preparation of Maitland and trypsinized tissue cultures. Virus was found in cultures of bone marrow and ovarian tissue, and less frequently in cultures of the lymph nodes, kidney and brain tissues; the tissue culture method was a less sensitive method than intracerebral inoculation of mice for the detection of small amounts of virus. The virus could be passaged in trypsinized cultures prepared from a number of different mouse organs, but in attempted passages with cultures of Maitland type only ovarian tissue supported continued multiplication of the virus. Most tissues were less susceptible to the virus than mouse brain. *D. J. Bauer*

Traub, E. & Schwöbel, W. Über die Immunität der weissen Maus gegenüber dem EEE-Virus. 2. Mitt.: Versuche mit Gewebekulturen. [**The Immunity of White Mice to Eastern Equine Encephalomyelitis Virus. II. Tissue Culture Experiments**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, Mar., v. 117, No. 3, 256–79, 2 figs. [24 refs.]

In mice infected with eastern equine encephalomyelitis virus subcutaneously and given a high-titre mouse immune serum intravenously 12 hours later a marked therapeutic effect of the serum was observed, and no virus could be found in the organs after 24 hours. Mouse kidney and lung cell cultures infected with the virus were treated with mouse immune serum in culture medium at intervals after infection, and after 48 hours the immune serum was removed and replaced with fresh culture medium. Some therapeutic effect was observed in the lung cell cultures. *D. J. Bauer*

Levkovich, E. N. & Zasukhina, G. D. **Serological Diagnosis of Tick-Borne Encephalitis by Tissue-Culture Method.** *Acta Virologica.* Prague. 1959, Apr., v. 3, No. 2, 73–81. [11 refs.]

The studies included 19 strains of Russian spring-summer encephalitis virus, 15 of them recent isolates. Human embryonic tissues in plasma clot cultures were used, as were trypsinized HeLa, cynomolgus monkey heart (CMH), monkey and dog kidney and human amniotic cells. Only human amniotic and monkey testicular cells failed to support virus multiplication.

Cultures reached their maximum virus titre between 3 and 8 days after inoculation. The highest titres were found in human embryonic skin-muscle, HeLa and CMH cells. Chick embryo and mouse embryo skin-muscle gave the lowest titres. The period before cytopathogenic changes occurred shortened with passage. Titres estimated in embryonic skin-muscle cultures did not differ significantly from estimates by titration in mice. 40 serial passages were achieved with the Sof'in strain. Neutralization tests in tissue culture and in mice were compared with acute and convalescent sera and no significant difference was detected. 40 sera were tested by a serum-dilution neutralization test in tissue culture and by a virus-dilution neutralization test in mice and the results were comparable. [But a clearer indication would have been obtained if the same type of test had been used in both hosts.] *C. E. Gordon Smith*

SHUBLADZE, A. K., BYCHKOVA, E. N. & ANAN'EV, V. A. **An Egg (Embryo) Vaccine for the Prophylaxis of Russian Spring-Summer (Tick) Encephalitis.** *J. Microbiol., Epidemiol. & Immunobiol.* London. 1958, v. 29, No. 10, 1642–9. [Translated from Russian.]

The vaccine consisted of a 10% suspension of chick embryo treated with 0·1% formalin. 8-day embryos were inoculated in the yolk sac and then incubated for 72 hours. The virus was said to have been unchanged by 20 to 30 passages in chick embryo. Immunogenicity of this vaccine is said to be as good as that of mouse brain vaccine, but simpler and cheaper to prepare. Inoculated human beings developed neutralizing antibodies and only transient local reactions are described.

The vaccine was prepared from 3 strains of virus, the Sof'in (after several 100 mouse passages) and 2 strains isolated in 1948 and 1949 (after 10 to 20 mouse passages). During 1949 and 1950, 16,000 persons in endemic areas were vaccinated and the effectiveness of the vaccine compared with controls is said to have been demonstrated [but no figures are given].

In [?] 1957 [1947 in the text appears to be in error] vaccines prepared in chick embryos gave protection indices varying from 32 to 93,000. With these vaccines, various concentrations of formalin at different temperatures for different periods of time were used in inactivation. 0·05% formalin for 5 days at room temperature followed by 15 days at 4°C., or 0·1% at 37°C. for 3 days were apparently effective. [The test of inactivation was apparently intracerebral inoculation of 20 mice with vaccine. This would not be considered adequate evidence of safety in the light of work on poliomyelitis vaccine.] 5% chick embryo vaccine dried in a mixture of 2% gelatin and 20% sucrose was found to be effective. When vaccines were freed of formalin by dialysis there was no loss of potency, but some vaccines found "safe" before removal of the formalin were found to contain live virus. Vaccines stored in the liquid state showed marked deterioration 2 to 7 months after preparation. The standard potency test prescribed by the Ministry of Health of the U.S.S.R. for these vaccines is the inoculation of 3 doses of 0·25 ml. of vaccine intraperitoneally into mice at 2-day intervals, followed by intracerebral challenge 2 weeks later.

Experiments have also been made on the growth of Russian spring-summer and Japanese encephalitis viruses in cultures of chick embryo skin-muscle fibroblasts. The culture fluids were found suitable as complement-fixing antigens and a vaccine for Russian spring-summer was successfully prepared.

C. E. Gordon Smith

FRANKLIN, R. M., WECKER, E. & HENRY, Claudia. **Some Properties of an Infectious Ribonucleic Acid from Mouse Encephalomyelitis Virus.** *Virology.* New York. 1959, Feb., v. 7, No. 2, 220–32, 1 fig. [18 refs.] [With an appendix on **The Infectivity Tests for Infectious Virus and Nucleic Acid,** 232–5, 3 figs.]

Phenol extracts prepared by the methods of GIERER and SCHRAMM [*Ztschr. f. Naturforsch.*, 1956, v. 11b, 138] and WECKER [see below] from the brains of mice infected with a strain of mouse encephalomyelitis virus had infectivity titres in mice of $1{\cdot}75 \times 10^2$ and $1{\cdot}3 \times 10^4$ per ml. The extracts contained both types of nucleic acid; their infectivity was greatly reduced by incubation with ribonuclease but was unaffected by deoxyribonuclease. Treatment of the infected brains with ribonuclease before extraction with phenol did not reduce the infectivity of the extract. Infective ribonucleic acid could also be extracted by phenol treatment from virus purified from mouse brain by fluorocarbon treatment, a finding which suggested that the infective nucleic acid was derived from the virus particles. The dose-response curve of infective ribonucleic acid in mice deviated from the theoretical curve expected from the Poisson distribution on the assumption that 1 unit of nucleic acid is sufficient to cause infection. but this deviation could be abolished by treatment of the material with deoxyribonuclease, or by purifying the ribonucleic acid by precipitation with molar sodium chloride.

D. J. Bauer

WECKER, E. **The Extraction of Infectious Virus Nucleic Acid with Hot Phenol.** [Correspondence.] *Virology.* New York. 1959, Feb., v. 7, No. 2, 241–3.

It has previously been found that infective ribonucleic acid can be extracted from cells infected with western equine encephalomyelitis virus with cold 80% phenol, but not from the purified and concentrated virus (*Ztschr. f. Naturforsch.*, 1957, v. 12b, 415; 1959 (in press)). In the present work the possibility of improving the extraction by using hot phenol has been investigated. In preliminary experiments with tobacco mosaic virus the yield of infective ribonucleic acid was greater when the extraction was carried out at 40°C. than at 4°C. A highly purified preparation of western equine encephalomyelitis virus containing $2{\cdot}5 \times 10^{10}$ PFU per ml. was shaken with an equal weight of phenol for 5 minutes at 40°C. or 50°C. The phases were then separated by centrifugation and the aqueous phase and interphase were removed and treated with phenol and an equal volume of buffer at the previous temperature. The phases were then separated and the treatment was repeated for the third time; the aqueous phase was then extracted with ether to remove phenol and aerated with nitrogen to remove the ether. By the extraction carried out at 40°C. 72 μgm. of infective RNA were obtained from 5 ml. of starting material, and at 50°C. the yield was 710 μgm.; the ribonucleic acids obtained at the 2 temperatures had infectivity titres of 2·35 and 3·24 log LD50 per ml. No ribonucleic acid could be obtained by extraction with phenol at 4°C.

D. J. Bauer

DIERCKS, F. H. & HAMMON, W. McD. **Hamster Kidney Cell Cultures in Laboratory Aspects of Epidemiologic Studies on Japanese B Encephalitis Virus.** *Proc. Soc. Exper. Biol. & Med.* 1959, Apr., v. 100, No. 4, 840–42.

24 sera from Southern Sumatra which had been previously tested in mice for neutralizing antibody to

Japanese encephalitis virus, were retested in a similar manner, but with hamster kidney cultures. The same sera were positive (neutralizing index >1·6 log) by each test.

Early mouse-brain passages of virus from Malaya and known infected mosquito suspensions from Japan were inoculated into hamster kidney cultures and into suckling mice and isolations were made from all by both methods. No virus was isolated by either method from infected human brain which had been frozen for 11 years. *C. E. Gordon Smith*

Diercks, F. H. & Hammon, W. McD. **Rate of Propagation of Japanese B Encephalitis Virus in Hamster Kidney Cell Cultures.** *Proc. Soc. Exper. Biol. & Med.* 1959, Apr., v. 100, No. 4, 722–6, 2 figs.

Tubes of hamster kidney cells were inoculated with 1,000 TCD50 of Japanese B encephalitis virus (Nakayama strain after 10 passages in hamster kidney cells). The virus content of the culture fluid was found to decrease for at least 6 hours, but by the 23rd hour an increase had occurred and infectivity increased logarithmically to about 10^7 TCD50 per 0·1 ml. after 69 hours. Tubes inoculated with only 10 TCD50 followed a similar multiplication curve about 1 log lower.

Tubes inoculated with 100 TCD50 of 25th passage virus showed minor cytopathic changes after 48 hours and marked changes after 72 hours. The virus content of such tubes was titrated at 24-hour intervals and maximum virus found between 72 and 96 hours after inoculation—thereafter the titre declined.

The virus content of the culture fluid of similar tubes was estimated hourly between the 45th and 52nd hours, between the 69th and 76th hours and between the 93rd and 100th hours after inoculation. The titres varied between 10^5 and 10^7 TCD50 per 0·1 ml.—the authors estimate that the accumulated dilution factor in these tubes at the 99th hour was 10^{-46}. It appears that most of the virus in these harvests had been released during the previous hour and as the increase of virus overnight over these hourly harvests is only about 1 log, the implication is that the rate of thermal degradation of virus is only a little less than the rate of multiplication. *C. E. Gordon Smith*

Chu, Kuan-Fu. **Application of the Interference Phenomenon in Tissue Culture for the Detection of Japanese B Encephalitis Virus.** *Acta Virologica.* Prague. 1959, Apr., v. 3, No. 2, 82–8, 4 figs. on 2 pls.

Fragments of chick embryo heart infected with Japanese encephalitis virus were grown in suspension for several days. Japanese encephalitis virus did not cause cytopathogenic changes in this tissue. The fragments were washed, then infected with Western equine encephalomyelitis virus and implanted in plasma clot in roller tubes. The tubes were examined daily for cytopathogenic changes presumed due to the Western equine virus. Such changes indicated failure of the Japanese encephalitis virus to multiply sufficiently to cause interference. The period of preliminary incubation with Japanese encephalitis virus depended on the dose of virus used. Japanese encephalitis antiserum inhibited the growth of the virus and therefore interference. Thus the phenomenon could be used to perform a neutralization test. *C. E. Gordon Smith*

Lavillaureix, J., Vermeil, C. & Petrovic, A. Note préliminaire concernant les caractères expérimentaux du virus West Nile. [**Preliminary Note on Experimental Characteristics of West Nile Virus**] *Bull. Soc. Path. Exot.* 1958, July–Aug., v. 51, No. 4, 486–9, 4 figs. on 2 pls.

Strain 28B of West Nile virus after 27 mouse passages was used. Intracerebral inoculation of mice caused death in 6 to 9 days. Viraemia was demonstrated and the virus was also found in the faeces of the mice. Intraperitoneal inoculation of mice aged less than 4 weeks caused death in about 14 days. Guineapigs were not affected by the virus, but viraemia and the formation of antibodies were demonstrated. Rabbits were insusceptible, but developed antibodies.

It was found possible to adapt the virus to gerbils after 1 blind passage intracerebrally. The incubation period in gerbils shortened to 4 to 5 days. Chicks aged less than a month developed encephalitis after intracerebral inoculation, while older chicks were not affected, but had viraemia and developed antibodies.

Histological studies were made of the tissues of these animals and signs of encephalitis similar to those caused by Japanese encephalitis were found.
C. E. Gordon Smith

Vermeil, C., Lavillaureix, J. & Reeb, E. Infection et transmission expérimentales du virus West Nile par *Ornithodoros coniceps* (Canestrini) de souche tunisienne. [**Infection and Experimental Transmission of West Nile Virus by a Tunisian Strain of *Ornithodorus coniceps***] *Bull Soc. Path. Exot.* 1958, July–Aug., v. 51, No. 4, 489–95. [16 refs.]

In 1953 *Ornithodorus coniceps* was found in a colony of gulls in Tunisia. It is known to occur in association with man and in houses in the centres of towns. The ticks were maintained on chicks, the larvae being fed under the wings which were strapped down for 3 to 15 days to prevent the birds from dislodging and eating the ticks. The strain 28B of West Nile virus was used and the ticks were infected by feeding them on viraemic chicks, guineapigs, mice and gerbils.

By grinding up the ticks and inoculating them into mice, virus was demonstrated in 3 groups of ticks. Later, ticks were permitted to bite mice and the brains of these mice were passaged into mice and into tissue cultures. Only 1 mouse appears to have been infected by bite and only this 1 was confirmed by blind passage in mice. However, blind passage in tissue culture appears to have demonstrated virus in every experiment. [Insufficient details are given to determine whether these isolations were identified as West Nile virus.]

The authors concluded that West Nile virus persisted

for at least 44 days in ticks fed on viraemic animals and that transmission by bite had been demonstrated.

C. E. Gordon Smith

THEIS, Gail A., BILLINGHAM, R. E., SILVERS, W. K. & KOPROWSKI, H. **Mechanism of Natural Resistance of Mice to Virus Infection.** [Correspondence.] *Virology.* New York. 1959, June, v. 8, No 2, 264–5.

PRI mice which are resistant to West Nile virus infection, and C_3H/St mice which are fully susceptible to it, were used. A proportion of PRI mice intravenously inoculated within 12 hours of birth with spleen or bone marrow cells from C_3H mice, became tolerant of C_3H tissue and were found to be more susceptible to West Nile virus than untreated PRI mice. To exclude the possibility that this was due to multiplication of the virus in the implanted C_3H cells, 6-thioguanine was used to treat PRI mice. These treated mice also became more susceptible to West Nile virus.

The authors concluded that these experiments seem to indicate that natural resistance to virus infection could be altered by partial impairment of function of the lymphoid tissue of the host.

C. E. Gordon Smith

NIKOLITSCH, M. Der Weg des neurotropen Virus, dargestellt in Modellversuchen an Tollwut und lymphozytärer Choriomeningitis. [**The Spread of a Neurotropic Virus, demonstrated in Model Experiments with Rabies and Lymphocytic Choriomeningitis Infection**] *Zent. f. Bakt.* I. Abt. Orig. 1959, v. 175, Nos. 1/2, 1–10.

In guineapigs infected intracerebrally with street rabies virus viraemia could not be detected at any stage of the infection, but virus was already present in the brain on the day after infection. With intramuscular infection virus appeared in the brain after 8 days and was absent from the blood throughout the incubation period of 11 days; it was therefore concluded that the virus cannot penetrate the intact blood-brain barrier. In similar experiments with lymphocytic choriomeningitis virus injected intracerebrally viraemia could be detected after 4 days, and in animals infected intramuscularly the virus was present in the blood on the 2nd day and appeared in the brain on the 4th day; it was therefore concluded that the virus can pass the blood-brain barrier in both directions. The viraemia after intracerebral infection could be prevented by the administration of immune serum but this treatment did not prevent the occurrence of viraemia after intramuscular infection.

D. J. Bauer

VILLEMOT, J. M. & PROVOST, A. Étude sur l'antigène soluble du virus rabique. [**Studies on Rabies Virus Soluble Antigen**] *Ann. Inst. Pasteur.* 1959, June, v. 96, No. 6, 712–22, 1 fig. [22 refs.]

[An abstract of this paper appeared in the *Tropical Diseases Bulletin*, 1959, v. 56, 1023.]

IMMUNITY

SULITZEANU, D. [**The Sites of Antibody Production**] *Harefuah.* Jerusalem. 1959, July 15, v. 57, No. 2 [In Hebrew 27–9. (10 refs.) English summary 29].

The English summary appended to the paper is as follows:—

"The site of antibody production has been the object of much research since the discovery of antibodies. Various organs were found capable of synthesis, foremost among them the spleen, bone marrow and lymphoid tissue.

"By using a double isotope labelling technique, it was possible to calculate the relative contributions of several organs to the total pool of circulating antibody and the turnover time of the intracellular antibody of these organs. It was found that the lung contained the largest amount of intracellular antibody and contributed the largest share to the serum pool. Bone marrow contained the second largest amount and the spleen contained only a small amount. However, the spleen antibody appeared to be synthesized at a faster rate than that of the lung."

LEON, M. A. & NORDÉN, Å. **Kinetics of Equine Complement.** *J. Immunology.* 1959, July, v. 83, No. 1, 99–104, 7 figs.

"1. Equine complement reacts with sensitized sheep erythrocytes to form a complex that can be lysed with EDTA treated guinea pig serum.

"2. The complex formed is more labile than the corresponding human or guinea pig complexes.

"3. The maximal concentration of complex obtained decreases to an asymptomatic value as the ratio of cells to equine serum is increased.

"4. At constant C'3, the lysis obtained is directly proportional to the concentration of complex."

SASLAW, S., BOURONCLE, Bertha A., WALL, R. L. & DOAN, C. A. **Studies on the Antibody Response in Splenectomized Persons.** *New England J. of Med.* 1959, July 16, v. 261, No. 3, 120–25, 2 figs. [20 refs.]

"The antibody response to subcutaneously administered tularemia vaccine in 92 of 105 splenectomized patients was similar to that observed in normal controls. It is more likely that the failure to exhibit antibodies in the remainder was due to the underlying disease than to the absence of the spleen. There was apparently no correlation between the serum protein electrophoretic pattern and the antibody response in either splenectomized or normal subjects."

STRAUCH, D., STENDER, H. S. & WINTER, H. **Effects of a Nonspecific Stimulation on Tissue Radiosensitivity during the course of Antibody Production.** *J. Immunology.* 1959, Apr., v. 82, No. 4, 298–303, 2 figs. [12 refs.]

It is known that antigen given before or shortly after total-body irradiation produces virtually normal immune responses, whereas antigen given more than 6

hours after irradiation elicits a greatly diminished amount of antibody. This subject was well reviewed recently by TALIAFERRO [this *Bulletin*, 1958, v. 33, 896].

The existence of a radiosensitive induction period in the immune response is generally agreed. The present work starts from the hypothesis that, since no radiosensitive phase can be demonstrated in animals exposed to antigen before X-rays, antigen-stimulation could be regarded as directly reducing the X-ray sensitivity of antibody-forming tissue (*i.e.* the reticulo-endothelial system).

Accordingly, rats were injected with carbon suspensions (as a non-specific stimulus) at varying times before or after exposure to X-rays; a single dose of *Br. melitensis* antigen was given 48 hours after irradiation, when considerable depression of immune response would be expected. However, rats which had received carbon 10 days or 5 days before irradiation showed an early rise and a greater total output of antibody than animals not given carbon. When carbon was given 1 hour after irradiation antibody production to *Br. melitensis* vaccine was as efficient as in non-irradiated rats. Histological studies showed a marked stimulation of lymphoid and reticulum cells as a result of carbon injection.

These findings are of considerable interest since they demonstrate clearly a new and logical concept of the radiosensitive phase in the immune response on which further studies must be based. Previously it has been thought [*e.g.* by DIXON *et al.*, this *Bulletin*, 1952, v. 27, (1078), *J. Immunology*, 1952, v. 68, 693] that, for normal response, irradiation must be preceded by antigen so that highly specific (and rather hypothetical) immuno-chemical "organizer" reactions can be set in train before tissue-damage occurs. From this paper it appears that the important role of antigen in this context is to act as a stimulus to reticulo-endothelial proliferation. Here antigen is not active as a specific agent and indeed its functions can be replaced carbon suspensions. *Derek Hobson*

KIND, Phyllis; JOHNSON, A. G.; WARD, P. A. **Studies on the Adjuvant Action of Bacterial Endotoxins on Antibody Formation. I. Time Limitation of Enhancing Effect and Restoration of Antibody Formation in X-Irradiated Rabbits** [KIND & JOHNSON]. *J. Immunology*. 1959, May, v. 82, No. 5, 415–27, 4 figs. [23 refs.] **II. Antibody Formation in Cortisone-Treated Rabbits** [WARD & JOHNSON]. *Ibid.*, 428–34, 3 figs. [18 refs.]

I. The endotoxins employed in this work were prepared from *Salmonella typhi* or *Escherichia coli* and the antigen used for production of antibody was a radio-iodinated preparation of human serum albumin. Endotoxin given before the injection of antigen failed to enhance antibody production whereas given within 2–3 days after it caused typical enhancement of antibody formation. Injections of endotoxin 24, 12 or 6 hours before antigenic stimulation showed no difference between test and controls, but the enhancement was evident in rabbits receiving endotoxin 6, 12, 24 or 48 hours after the injection of the human serum albumin. It would appear that X-irradiation before and immediately after antigenic stimulation can impair antibody formation but that endotoxin may affect positively this early critical step in antibody production which has been depressed by the radiation.

II. There have been many reports concerning the inhibitory effect of cortisone on the antibody response in rabbits to the injection of various antigens, but detailed information about the means by which cortisone exerts this effect is by no means clear and several of the results of experiments designed to answer this question have been contradictory. In general, however, it appeared that the exhibition of cortisone immediately before, and for some days after, the injection of bacterial endotoxins, did affect the early primary response. When the authors re-examined this problem with similar experiments by the initiation of cortisone treatment one day before the intravenous injection of the endotoxin and continuing it daily for 11 days, they found that antibody formation, as measured by antigen elimination techniques, began 2 days after the cessation of cortisone treatment. 9 weeks later the reinjection of a very small dose of endotoxin resulted in a typical rapid secondary response. It would appear therefore that the inhibitory effect of cortisone on the primary response is probably exerted early in the sequence of events leading to antibody synthesis. Variations in time of initiation and duration of cortisone treatment did affect the secondary response, but in only about 50% of the animals. [It may be of interest to recall that SHEWELL and LONG [this *Bulletin*, 1957, v. 32, 295] showed that impairment of antibody synthesis in animals under treatment with cortisone was limited to those termed cortisone-sensitive—rats, mice, rabbits and ferrets. Man, rhesus monkeys and guineapigs under heavy cortisone dosage do not show reduced capacity in the formation of antibody.] *H. J. Bensted*

SCHIFF, W. Untersuchungen zum Seemüller-Phänomen. I. Mitteilung. Hämagglutinin-Bindung *in vitro* und intravitale Hämolyse. [**Investigation on the Seemüller-Phenomenon. I. Haemagglutinin *in vitro* Binding and Intravital Haemolysis**] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, July, v. 118, No. 1, 36–56, 4 figs. [24 refs.]

MCVICKAR, D. L. & WEINFELD, Gertrude, R. **Immune Hemolysis at 0°: I. Introduction: The Role of Amboceptor and Complement.** *J. Immunology*. 1959, Apr., v. 82, No. 4, 290–97, 6 figs. [13 refs.]

It is generally believed that red blood cells (E) optimally sensitized with haemolytic antibody (A) react readily with the complement components C′1 and C′4 at 0°C. or at higher temperatures, provided optimum concentrations of calcium are present. C′2 then reacts with the complex EAC′1·4, if magnesium is present in optimum amounts; again the reaction proceeds equally readily at 0°C. The complex EAC′1.4.2. can interact with C′3 only at temperatures greater than 15°C.,

though the final complex EAC'1.4.2.3., once formed, can proceed to haemolysis at 0°C.

This hypothesis, originating largely from the work of MAYER and his colleagues [*e.g.* LEVINE and MAYER, *J. Immunology*, 1954, v. 73, 426; this *Bulletin*, 1955, v. 30, (451)] remains a reasonably satisfactory explanation of complement behaviour, and fits most of the experimental data accumulated by most workers over many years. Recently, however, as the minutiae have been re-examined, minor deviations from the hypothesis have been found, and are reported in several recent papers [*e.g.* RAPP, this *Bulletin*, 1958, v. 33, 540; AMIRAIAN *et al.*, *ibid.*, 541].

In the present study it has been shown that erythrocytes, sensitized with greater than optimum amounts of antibody, can proceed to complete haemolysis in the presence of C' at a temperature of 0°C. throughout. The kinetics of the reaction at different multiples of the optimum sensitizing dose were studied, but no further analysis of the reactions was presented in support of various hypotheses which are discussed. The most likely of these is that C'3 utilization by EAC'1.4.2. is increased at 0°C., and that the factor responsible for this improved uptake is an increased concentration of antibody molecules on the erythrocyte surface. It is possible that closely-adjacent EAC'1.4.2. groups on the cell-surface may cooperate in taking up C'3.

A possible practical application of this study is that it presents a method of studying immune haemolysis throughout at a constant low temperature. This may be of value in avoiding the marked instability of intermediate protein-containing complexes of the reaction which normally renders quantitative studies difficult.

Derek Hobson

PLESCIA, O. J., CAVALLO, G., AMIRAIAN, K. & HEIDELBERGER, M. **Aspects of the Immune Hemolytic Reaction. IV. Inhibition of Hemolysis by the Reaction Products.** *J. Immunology*. 1958, May, v. 80, No. 5, 374–81, 1 fig. [13 refs.]

The extent of haemolysis of sensitized erythrocytes by complement (C') is partly determined by the operation of inhibitory secondary reactions such as thermal inactivation of C', or anticomplementary constituents of serum. The present paper investigates the extent to which products of the immune haemolytic process itself can inhibit further haemolysis.

When sensitized sheep erythrocytes were lysed by pig C', the stromata accounted for almost all the anticomplementary activity of the lysate; guineapig C' was also inhibited by this product. Stromata prepared from normal non-sensitized erythrocytes had no inhibitory effect, and it appeared that the sensitizing antibody was essential for the reaction. It was shown that sensitized stromata did not continue to fix C' components in the same manner as the original sensitized red blood cell; C'2 and C'4 were markedly reduced in titre, but C'1 and C'3 were little affected. The degree of deviation of C' components by sensitized stromata depended upon temperature, but at 37°C. was sufficiently large to influence the general pattern of haemolysis in a well-defined system.

Various hypotheses were put forward to explain this phenomenon but none was submitted to experiment in this paper; the most reasonable explanation would seem to be that sensitized stromata produce competitive substrates for proteolytic components of C'.

Derek Hobson

BANOVITZ, J.; SINGER, S. J.; WOLFE, H. R. **Precipitin Production in Chickens. XVIII. Physical Chemical Studies on Complexes of Bovine Serum Albumin and its Chicken Antibodies** [BANOVITZ, SINGER & WOLFE]. *J. Immunology*. 1959, June, v. 82, No. 6, 481–8, 5 figs. [14 refs.] **XIX. The Components of Chicken Antiserum involved in the Precipitin Reaction** [BANOVITZ & WOLFE]. *Ibid.*, 489–96, 4 figs. [10 refs.]

WARDLAW, A. C. & PILLEMER, L. **Inhibition of the Bactericidal Activity of the Properdin System by Zymosan and Other Properdin Binding Agents.** *J. Immunology*. 1959, Apr., v. 82, No. 4, 313–18, 1 fig.

The insoluble yeast polysaccharide zymosan is highly effective in absorbing properdin from serum, and by strict control of time and temperature of adsorption this can be achieved without significant loss of complement (C') components [PILLEMER *et al.*, this *Bulletin*, 1955, v. 30, 83]. Serum deprived of properdin by this method loses the normal bactericidal activity against Gram-negative organisms.

Other polysaccharides of high molecular weight and components of microbial cell walls are known to combine with properdin, and the present paper reports investigations of their efficiency in preventing the bactericidal activity of serum.

When the reagent under test was added to serum at the same time as a properdin-sensitive organism (*Shigella dysenteriae*), inhibition of bactericidal activity was much greater for reagents known to inactivate complement in addition to properdin-adsorption than for reagents capable of combination with properdin alone. 3 dextrans in clinical use failed to reduce bactericidal activity.

When, on the other hand, each reagent was allowed to react with serum alone and the resulting adsorbed product was subsequently tested, all were shown to have almost equal efficiency in achieving 99% removal of properdin without simultaneous loss of C' components. In all cases the bactericidal activity of the product was lost, but could be restored by addition of purified properdin. The anomalous results of competitive inhibition tests and adsorption tests could be explained by differences in reaction rates.

[The most important aspect of this paper is the demonstration that zymosan can be replaced by materials derived from a wide variety of microbial sources. This adds further support to the view that properdin is a normal serum component resembling antibody in that it forms a bactericidal system with C', but differing in its wide range of serological activity.] *Derek Hobson*

HEYMANN, G. & WAHLIG, H. Properdin-Spiegel und Antikörperbildung bei Kaninchen während der Immunisierung mit *Mycobacterium tuberculosis* und *Salmonella typhosa*. [**Properdin Level and Antibody Production in Rabbits during Immunization with** *Mycobacterium tuberculosis* **and** *Salmonella typhosa*] *Ztschr. f. Immunitätsf. u. Exper. Therap.* 1959, July, v. 118, No. 1, 57–72, 6 figs. [32 refs.]

The method of determining the properdin content of serum is modelled on that of MCNALL (*Proc. Soc. Exper. Biol. & Med.*, 1957, v. 94, 399) with the modification that zymosan is used rather than inulin in the neutralization of the third component of complement.

Groups of rabbits were immunized with 6 doses of suspensions of *Myco. tuberculosis* and *Salm. typhi* respectively and determinations were made of the properdin levels, development of antibody and of the variations in the protein content of the sera as determined by electrophoresis.

These observations showed that there was a sharp rise in properdin content of serum which followed within 48 hours of the beginning of immunization with both bacteria. A decline ensued and afterwards a second rise, reaching its summit about the ninth day in the case of the typhoid inoculation and considerably later with inoculation of the mycobacteria. In both cases the second summit was followed by a gradual return to normal level.

Development of antibody occurred more gradually, becoming marked in the second week and continuing, but rather more slowly, thereafter. There was a good correlation between increase of gamma globulin and development of antibody.

Mycobacteria appear, like zymosan, to form a complex with properdin which throws the third component of complement out of action.

The authors draw attention to the possibility that a period of special danger exists in the early course of immunization when the properdin content of the serum has fallen and antibody formation is not yet increased.

They do not consider that their observations establish that properdin plays a part in the development of immunity. *J. W. McLeod*

GLEDHILL, A. W. **The Effect of Bacterial Endotoxin on Resistance of Mice to Ectromelia.** *Brit. J. Exper. Path.* 1959, Mar., v. 40, No. 2, 195–202, [12 refs.]

Endotoxin intraperitoneally or saccharated iron oxide intravenously increased the survival time of weanling mice (strain TO) which subsequently received a large dose of ectromelia virus (10^6 LD50). On the other hand a smaller dose (10^3 LD50) reduced the survival time of animals pretreated with endotoxin; and 1 LD50 injected into animals which received endotoxin gave a mortality of 95% compared with 55% in controls. (The endotoxins used were prepared from *Chromobacterium prodigiosum* and *Salmonella typhi-murium*.)

The lethal effect of ectromelia virus in normal and in endotoxin-pretreated mice of 2 strains of mice was examined. In strain TO, endotoxin increased susceptibility to a level comparable with that in untreated strain VS mice. The susceptibility of strain VS mice was not increased by endotoxin.

The author suggests that the short but significant increase in the survival time of endotoxin-pretreated mice receiving very large doses of virus is the result of stimulation of the reticulo-endothelial system which clears the blood more effectively thereby lessening the invasion of the vital structures, such as the liver parenchyma. He suggests that stimulation of the reticulo-endothelial system may also account for increased susceptibility to smaller doses on the hypothesis that virus multiplication will take place more readily within the cells of the system [see also this *Bulletin*, 1959, v. 34, 296]. *Douglas D. Smith*

OSLER, A. G., RANDALL, H. G., HILL, Betsy M. & OVARY, Z. **Studies on the Mechanism of Hypersensitivity Phenomena. III. The Participation of Complement in the Formation of Anaphylatoxin.** *J. Exper. Med.* 1959, Aug. 1, v. 110, No. 2, 311–39, 10 figs. [81 refs.]

MATSUBARA, H., MAYEDA, A., TANABE, S. & SHICHIKAWA, K. Étude immunologique de la polyarthrite chronique évolutive sur la production expérimentale du facteur activateur d'agglutination. [**Immunological Study of Rheumatoid Arthritis. Experimental Production of the Agglutination Activating Factor**] *Ann. Inst. Pasteur.* 1959, Aug., v. 97, No. 2, 218–26. [24 refs.]

The English summary appended to the paper is as follows:—

"In sera of rabbits immunized with *Salmonella pullorum* or with streptococci the authors have demonstrated the presence of a factor which activates the agglutination of sensitized red cells. They describe the properties of this factor and compare them with those of the A.A.F. present in the sera of rheumatoid arthritis patients."

Book Reviews

MEDICAL RESEARCH COUNCIL. **Report of the Medical Research Council for the Year 1957–1958.** Cmnd. 792. pp. viii + 288, 5 figs. (4 on 4 pls.) 1959. London: H.M. Stationery Office. [13s.]

This Report of the Medical Research Council for the year 1957–8 "follows the pattern used in recent years". It contains summaries of the very numerous researches carried out under the auspices of the Council in many places and much general information which includes also lists of references to the scientific publications in which individual workers have given full accounts of their researches.

Of particular and absorbing interest are the 11 articles presented under the heading *Some Aspects of Medical Research* which are reprinted separately under the title *Current Medical Research* (H.M.S.O., price 3s. 6d.). These are on selected aspects of the wide field of medical research and are general surveys of research on a particular subject. In order to give a reasonably balanced and just picture of research on each subject in these articles, references are made not only to the Council's work but sometimes extensively to research initiated or developed elsewhere.

Preceding these articles is a short report on "The Council's Laboratories in West Africa" in which the development of research in the Gambia is shortly described.

The Hyperendemic Malaria of the Gambia

The general patterns of health and mortality of infants and young children in the Gambia broadly resemble those reported from comparable territories in tropical Africa. Mortality rates are high and general health unsatisfactory. The Gambian child in the first 2 years of life when innumerable other hazards to health are also encountered is almost continuously infected with malaria, yet overt clinical illness of malaria develops only intermittently. In this situation several questions arise which were investigated by study of the effect of prophylaxis by antimalarial drugs in childhood, gamma globulin levels in relation to malarial infection and disease and liver enlargement in childhood due to malaria in relation to hepatic function. It would appear from these preliminary investigations, if confirmed, that in African territories where eradication of hyperendemic malaria is at present impracticable judicious antimalarial drug treatment of children under 3 years could result in the saving of life and improvement in health.

Intracellular Organelles

The functional units of the animal cell—nucleus, mitochondria and numerous smaller granules bathed in the cell sap are commonly referred to as the cell organelles or organoids. Much has been learnt about cell structure by the ordinary microscope, phase contrast microscopy and the electron microscope. By the development of the technique of differential centrifugation, in which the cells suspended in an isotonic fluid are first mechanically disrupted and then submitted to centrifugation at different rates, 4 main fractions can be prepared from the broken cells. "The first two, the nuclear and mitochondrial, correspond reasonably well to the cellular organelles as they are in the cell." The third fraction, the "microsomal," probably consists mainly of broken intracellular membranes and the fourth is the extraparticulate fluid of the cell diluted with the homogenizing fluid. This article reviews clearly the important results which have already been obtaind by the study of the chemical constitution and enzymic properties of these isolated cellular fractions.

The Viruses of Trachoma and Inclusion Blennorrhoea

"Trachoma is the greatest single cause of blindness and impaired vision in the world." This article gives an account of the isolation of viruses from cases of trachoma in Peking by T'ANG and his colleagues in 1957, the confirmation of this work in London and later the isolation of African strains of trachoma from patients in the Gambia. That this virus was the cause of trachoma was proved by the development of typical trachoma in a blind volunteer whose conjunctiva was inoculated with virus from the 8th serial egg passage of 1 of the African viruses. The virus of inclusion blennorrhoea may also have been isolated by the same technique as that used for the trachoma virus but the final identification of this agent must await the result of a human inoculation experiment.

Progress towards Cultivation of the Leprosy Bacillus

Leprosy is no longer an endemic disease in Northern Europe yet recent estimates suggest that there are 10 to 15 million cases in the world to-day, of which about one-third are in countries of the British Commonwealth. This article describes some of the history of study of the leprosy bacillus and the results of recent experiments which have demonstrated that multiplication of the allied bacillus of rat leprosy occurs *in vitro* in the presence of fibroblasts. It is hoped that fundamentally similar methods may secure success with the human leprosy bacillus which has never been cultivated *in vitro* since it was first recognized 56 years ago.

Colicine Typing in the Epidemiological Study of Sonne Dysentery

"Many attempts to type Sonne cultures have been made, but, until recently, with little success." In 1954, however, the sensitivity or resistance of Sonne strains to sulphonamides was found to be a reliable epidemiological "marker". Recently a method of typing based upon the production of colicines has been reported which has given useful epidemiological information. In 1946 the term "colicine" had been coined for "the antibacterial substances elaborated by many strains of *Bact. coli*" which inhibited the growth of another strain of the same organism. The term has been extended to include similar substances produced by other intestinal bacteria. A high proportion of cultures of *Sh. sonnei*

were found to produce colicines active against other strains.

Cancer-producing Viruses and their Immunology

"Within the last eight years research work, initiated in the United States, has brought about a dramatic advance in our knowledge of the relationships between viruses and cancer." This short but informative article contains a review of recent work on cancer-producing agents in cell-free tissue extracts, the tissue culture of a cancer-producing virus, the antigenic relationships of the cancer-producing viruses, tumour viruses and acquired immunological tolerance and the nature of cancer-producing viruses.

Ultramicro-analysis

Only in recent years have techniques been developed which are capable of detecting quantities of substances as small as a millimicrogramme (10^{-9} of a gm.) or even a micromicrogramme (10^{-12} of a gm.), with an error of $\pm$ 5%. Brief descriptions are given in this article of the different techniques employed in the analyses of fluid from the inner ear, the cerebrospinal fluid and the blood. In the first of these examples samples of the labyrinthine fluid of not more than 0·2 to 0·5 microlitre were available yet accurate estimations of protein and non-protein nitrogen, sodium, potassium, calcium and magnesium could be made.

The Performance of Coal Miners in Hot Atmospheres

In this article there is an account of some of the work which has been carried out on the limiting conditions of the thermal environment for sustained work, for the normal working day in mining and for short exposures as in mines rescue work. The conclusion is that the limits of human tolerance to specified conditions, as in rescue work, can be established experimentally without difficulty but the assessment of the effects of daily exposure to heat over many years will require a long series of carefully controlled investigations.

Research in General Practice

Medical practitioners have made many contributions to knowledge and in this article there is mention of the achievements of Hippocrates, Thomas Sydenham, John Fothergill, William Budd, Edward Jenner, James Mackenzie and William Pickles. In spite of the limitations implicit in general practice as it exists to-day there is a widespread feeling that research in general practice may still make substantial contributions to medical knowledge. There is a brief account of recent research in general practice supported by the Medical Research Council and also by other bodies in Britain and in the United States.

Mammalian Fertilization

In the last few years considerable advances have been made in knowledge of the complexities of mammalian fertilization and these are well reviewed in this article. There are short references to the prevention of "polyspermy" or the penetration of an excessive number of spermatozoa into the ovum, an event that almost certainly condemns the embryo to an early death. The remarkable results of studies on (1) the penetration of the spermatozoon into the egg, (2) the structural changes in living eggs during fertilization, (3) chemical changes in fertilization, and (4) the induction of anomalous forms of fertilization and parthenogenesis are shortly but very clearly described.

Rehabilitation of Chronic Schizophrenics

The Council's Social Psychiatry Research Unit has carried out 2 investigations into "the psychological and social processes involved in re-training chronic schizophrenics and effecting their resettlement in the general community". It was found that both paranoid and non-paranoid patients could perform simple industrial work and that with prolonged initial training could approximate to the rate of work of normal unskilled persons. They differed from normal persons in that they "appeared to be relatively unaffected by the usual forms of social incentive"; and also would seem on the evidence to react "adversely to receiving close personal attention during the performance of the task". This evidence and that obtained by study after re-settlement reflects "the need of schizophrenics to preserve a 'social distance' protecting them from close personal interaction". *M. E. Delafield*

ELKINS, Hervey B. **The Chemistry of Industrial Toxicology.** 2nd Edition. pp. xi + 452, illustrated. 1959. New York: John Wiley & Sons, Inc. London: Chapman & Hall Ltd., 37, Essex Street, W.C.2. [92s.]

In the second edition of this book, as in the first, special emphasis is laid on the chemical and engineering aspects of industrial problems, but early chapters provide also a straightforward account of the properties and physiological and pathological effects of many industrial materials, both those already well recognized as toxic and also others which have during recent years become increasingly important, notably the radio-active isotopes. A valuable feature of the presentation of these chapters is the inclusion of tables showing the composition of mixtures of substances used in various industrial operations and the vapour concentrations of each; the narcotic concentrations of different members of the same group; and enumeration of the biological analyses used as aids to the evaluation of their toxicity.

The section on Preventive Measures is rather disappointingly inadequate in a book of this calibre, though the author does state that only the fundamental principles are outlined. The note on protective creams, for example, merely states that their application is often advocated and somewhat less frequently carried out successfully—not a very informative contribution to what is already known of this method of skin protection.

The chapter on Industrial Operations and Processes, however, contains much valuable information on the methods of handling materials used in a wide range of industrial processes and the chief hazards to be expected, with tables of the actual concentrations found both of metals and solvents. The tabular summary of operations

and hazards includes such relatively rarely described processes as " condenser impregnating ", " indoor trucking ", " multigraphing " and " laboratory work ".

A very clear account is given of the problems of Maximum Permissible Concentrations [MAC], with the illuminating remark that the camel of difficulty in applying the results of animal tests to human beings is more easily swallowed than the gnat of varying susceptibility. The table in this section includes not only the MAC recommended by the American Conference of Governmental Hygienists of 1957 and by Imperial Chemical Industries in 1952 but also some of the author's own suggestions. These are sometimes in agreement with those generally accepted, in a few cases they differ considerably; the discrepancies are presumably based on criteria formulated from personal experience.

It is in the sections dealing with the procedures and instruments used for detecting, analysing and estimating toxic materials in air and urine, and with biological examinations for evidence of systemic disturbance that the unique value of this book is perhaps most apparent. The concise accounts, arranged in alphabetical order, of a large number of toxic materials, with descriptions of the methods, reagents and instruments used for biological estimation of their metabolic products, explore even the relatively little-known field of radio-activity—for example, the estimation of radium and plutonium in urine.

There is an extensive bibliography of 555 publications. While the medical toxicologist will find much of interest and value in this book, to the chemist and chemical engineer it will prove an indispensable source of reference in the investigation of problems connected with the detection and prevention of ill-health due to occupational hazards. *Ethel Browning*

BERGER, E. & MELNICK, J. L. [Edited by.] **Progress in Medical Virology. Vol. 1.** 304 pp., numerous figs. 1958. Basle. New York: S. Karger. [78s.]

Viruses are becoming of increasing importance in biological science. Great technical improvements are leading to swift advances in knowledge. Cellular pathology, genetics and the study of infectious diseases are all benefiting from the vigour of the science of virology. The flood of original articles is such as to overwhelm even the professional in all but his narrow field. There is, therefore, a great need for authoritative comprehensive review articles to digest and present a coherent account of the new information. This is required both for the specialist and even more so for colleagues in related spheres. There is a particular need for a series dealing with the applications of the new knowledge in medicine particularly in the fields of public health and epidemiology. A new annual international series entitled *Progress in Medical Virology* with distinguished editors and an impressive list of contributors is, therefore, very welcome.

The editors do not seem to have decided at what audience to direct their contributors. Some of the authors in an attempt to remain absolutely up to date have referred to work not yet published. Such efforts are vain as newer publications will inevitably render a review out of date and the great part of the value of a review is lost if it fails to lead the enquiring reader to the original work. There are two interesting accounts of the power of modern virology in the investigation of recent outbreaks of epidemic disease (Asian influenza by K. E. JENSEN, F. L. DUNN, and R. Q. ROBINSON, pp. 165–209; and Kyasanur Forest disease by T. H. WORK, pp. 248–79) [see also this *Bulletin*, 1958, v. 33, 444] which suffer from this defect. Kyanasur Forest disease is a recently encountered variety of disease due to Russian spring-summer encephalitis virus in India which appears to be closely similar to Omsk haemorrhagic fever. There is a more definitive account of tick-borne spring-summer encephalitis by A. A. SMORODINTSEV (pp. 210–47). J. H. S. GEAR (pp. 106–21) has written an excellent account of the recently described serious infections of new-born infants with Coxsackie B viruses. Also dealing with medical applications is a comprehensive account of the difficulties encountered by one manufacturer in the preparation of poliovaccine. The methods employed to obtained a consistently safe and potent vaccine are outlined (I. W. MCLEAN, Jr. and A. R. TAYLOR, pp. 122–64).

The other contributions are of more strictly virological interest dealing with the role of nucleic acid in virus infections (J. S. COLTER, pp. 1–35); viral carrier states in tissue culture (H. S. GINSBERG, pp. 36–58); a comprehensive treatment of the Enterovirus group (J. L. MELNICK, pp. 59–105); and an account of the increasing importance of direct flocculation techniques in the study of virus antigen and antibody reactions (WILSON SMITH, pp. 278–304). *A. J. Beale*

Printed in Great Britain by The Eastern Press, Ltd., London and Reading